

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Billy D. Chism Examiner #: 79291 Date: 23 August 2002  
 Art Unit: 1453 Phone Number 306-5815 Serial Number: 09/767633  
 Mail Box and Bldg/Room Location: \_\_\_\_\_ Results Format Preferred (circle): PAPER DISK E-MAIL

CM19801/9D12

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Methods of treating Diabetic cardiomyopathy using glycogen phosphorylase inhibitors.  
 Inventors (please provide full names): Judith L. Treadway (2)

Earliest Priority Filing Date: 01/24/2000 (3)

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search the attached compound (4) in conjunction with the following key words: In particular the attached compound names.

1. glycogen phosphorylase inhibitor.

2. diabetic (6)

3. diabetes

4. cardiovascular

5. heart (7)

6. ischemia (myocardial)

7. reperfusion

Thank You,

Billy D. Chism

Point of Contact:  
 Thomas G. Larson,  
 703-308-7309  
 CM1, Rm. 6 B 01

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 AUG 23 2002  
 ECH/CHEN DIVISION  
 (STIC)

Point of Contact:  
 Thomas G. Larson, Ph.D.  
 703-308-7309  
 CM1, Rm. 6 B 01

## STAFF USE ONLY

## Type of Search:

## Vendors and cost where applicable

Searcher: Point of Contact:  
Thomas G. Larson, Ph.D.  
 Searcher Phone #: 703-308-7309  
 Searcher Location: CM1, Rm. 6 B 01

NA Sequence (#) \_\_\_\_\_

STN 41402

AA Sequence (#) \_\_\_\_\_

Dialog \_\_\_\_\_

Date Searcher Picked Up: \_\_\_\_\_

Structure (#) 8

Questel/Orbit \_\_\_\_\_

Date Searcher Completed: 9/5Bibliographic ☒

Dr. Link \_\_\_\_\_

Date Completed: 120

Litigation \_\_\_\_\_

Lexis/Nexis \_\_\_\_\_

Searcher Prep & Review Time: 120

Fulltext \_\_\_\_\_

Sequence Systems \_\_\_\_\_

Clerical Prep Time: \_\_\_\_\_

Patent Family \_\_\_\_\_

WWW/Internet \_\_\_\_\_

Online Time: 330

Other: \_\_\_\_\_

Other (specify) \_\_\_\_\_

Methods for making the above recited glycogen phosphorylase inhibitors of Formula A can be found in U.S. provisional patent application number 60/157,148, filed September 30, 1999.

Commonly assigned PCT published applications [WO 96/39384 and WO 96/39385] disclose glycogen phosphorylase inhibitors of Formulas I and IA below that can be used to treat diabetic cardiomyopathy in accordance with the present invention.

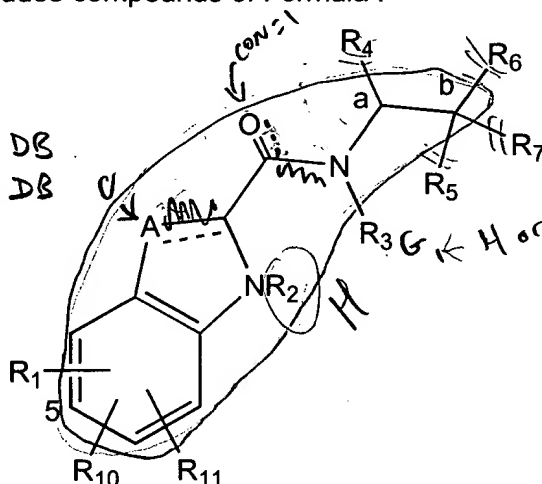
One group of glycogen phosphorylase inhibitors that can be used in the present invention includes compounds of Formula I

RID =

333.151.57 w DB

" " .54 w/o DB

Indole



Formula I

and the pharmaceutically acceptable salts and prodrugs thereof wherein

the dotted line (---) is an optional bond;

15 A is -C(H)=, -C((C<sub>1</sub>-C<sub>4</sub>)alkyl)= or -C(halo)= when the dotted line (---) is a bond, or A is methylene or -CH((C<sub>1</sub>-C<sub>4</sub>)alkyl)- when the dotted line (---) is not a bond;

R<sub>1</sub>, R<sub>10</sub> or R<sub>11</sub> are each independently H, halo, 4-, 6- or 7-nitro, cyano, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy, fluoromethyl, difluoromethyl or trifluoromethyl;

R<sub>2</sub> is H;

20 R<sub>3</sub> is H or (C<sub>1</sub>-C<sub>5</sub>)alkyl;

R<sub>4</sub> is H, methyl, ethyl, n-propyl, hydroxy(C<sub>1</sub>-C<sub>3</sub>)alkyl, (C<sub>1</sub>-C<sub>3</sub>)alkoxy(C<sub>1</sub>-C<sub>3</sub>)alkyl, phenyl(C<sub>1</sub>-C<sub>4</sub>)alkyl, phenylhydroxy(C<sub>1</sub>-C<sub>4</sub>)alkyl, phenyl(C<sub>1</sub>-C<sub>4</sub>)alkoxy(C<sub>1</sub>-C<sub>4</sub>)alkyl, then-2- or -3-yl(C<sub>1</sub>-C<sub>4</sub>)alkyl or fur-2- or -3-yl(C<sub>1</sub>-C<sub>4</sub>)alkyl wherein said R<sub>4</sub> rings are mono-, di- or tri-substituted independently on carbon with H, halo, (C<sub>1</sub>-C<sub>4</sub>)alkyl, (C<sub>1</sub>-C<sub>4</sub>)alkoxy,

25 trifluoromethyl, hydroxy, amino or cyano; or

Claims

What is claimed is:

1. A method of treating diabetic cardiomyopathy, the method comprising  
5 administering to a patient having or at risk of having diabetic cardiomyopathy a therapeutically effective amount of a glycogen phosphorylase inhibitor.
2. The method of claim 1 wherein the glycogen phosphorylase inhibitor is selected  
10 from 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxy-dimethylcarbamoyl-methyl)-2-phenyl-ethyl]-amide; (1)  
✓ 5,6-dichloro-1H-indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide; (2)  
✓ 5-chloro-1H-indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methoxy-methyl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide; (3)  
15 ✓ 5-chloro-1H-indole-2-carboxylic acid ((1S)-{(R)-hydroxy-[(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl}-2-phenyl-ethyl)-amide; (4)  
✓ 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxy-pyrrolidin-1-yl)-(2R)-hydroxy-3-oxo-propyl]-amide; (5)  
✓ 5-chloro-1H-indole-2-carboxylic acid {(1S)-[(R)-hydroxy-(methyl-pyridin-2-yl-carbamoyl)-methyl]-2-phenyl-ethyl}-amide; or (6)  
20 ✓ 5-chloro-1H-indole-2-carboxylic acid ((1S)-{(R)-hydroxy-[methyl-(2-pyridin-2-yl-ethyl)-carbamoyl]-methyl}-2-phenyl-ethyl)-amide, or a pharmaceutically acceptable salt or prodrug thereof, or a salt of a prodrug. (7)
- 25 3. A method of treating diabetic cardiomyopathy, the method comprising administering to a patient having 1) diabetes and 2) cardiovascular disease, ischemic heart disease, congestive heart failure, congestive heart failure but not having coronary arteriosclerosis, hypertension, diastolic blood pressure abnormalities, microvascular diabetic complications, abnormal left ventricular function, myocardial  
30 fibrosis, abnormal cardiac function, pulmonary congestion, small vessel disease, small vessel disease without atherosclerotic cardiovascular disease or luminal narrowing, coagulopathy, cardiac contusion, or having had or at risk of having a myocardial infarction a therapeutically effective amount of a glycogen phosphorylase inhibitor.

Fig #9  
From  
WO docs

Search for Species of claim 2. CAS Registry Nos.  
used in search were obtained from Inventors' priority  
documents, WO 96/39384  
and WO 96/39385. B. Chism; 09/767,633

Page 1

=> D QUE L32

L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR  
PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI  
L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)  
L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT  
OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR  
PKT OR DMA)/RL  
L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT  
OR DIABETES MELLITUS+NT,PFT/CT  
L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC  
CARDIOMYOPATHY"+PFT/CT  
L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/C  
T  
L7 20270 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOP  
ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT  
OR ISCHEMIA+NT,PFT/CT  
L8 9348 SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR  
"REPERFUSION (L) INJURY"+PFT/CT  
L9 335374 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6  
OR L7 OR L8)  
L10 1 SEA FILE=REGISTRY ABB=ON PLU=ON 186392-40-5/RN  
L17 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L10  
L24 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L17  
L31 2 SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR  
PN  
L32 8 SEA FILE=HCAPLUS ABB=ON PLU=ON L24 NOT L31

Claim 2, 1st compound  
CAS Reg. No.  
WO199639385/ - Remove  
inventors' priority documents  
from answer set.

=> FIL REG

FILE 'REGISTRY' ENTERED AT 11:56:46 ON 05 SEP 2002  
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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3  
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L10

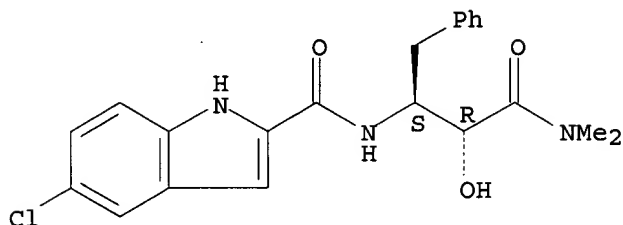
L10 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
RN 186392-40-5 REGISTRY  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-  
oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[3-(dimethylamino)-2-hydroxy-3-oxo-1-  
(phenylmethyl)propyl]-, [R-(R\*,S\*)]-  
OTHER NAMES:

Point of Contact:  
Thomas G. Larson, Ph.D.  
703-308-7309  
CM1, Rm. 6 B 01



CN CP 91149  
FS STEREOSEARCH  
MF C21 H22 Cl N3 O3  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

10 REFERENCES IN FILE CA (1967 TO DATE)  
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

FILE 'HCAPLUS' ENTERED AT 11:57:07 ON 05 SEP 2002  
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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10  
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L32 1-8

L32 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:709687 HCAPLUS  
DOCUMENT NUMBER: 135:272869  
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes

*Hits from CAPLUS with  
compound 2 key words*

INVENTOR(S): Treadway, Judith Lee  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: Eur. Pat. Appl., 78 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319

PRIORITY APPLN. INFO.: US 2000-191381P P 20000322

OTHER SOURCE(S): MARPAT 135:272869

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH<sub>2</sub>, CH-alkyl when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6- or 7-NO<sub>2</sub>, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R<sub>2</sub> = H; R<sub>3</sub> = H, alkyl; R<sub>4</sub> = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R<sub>5</sub> = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R<sub>7</sub> = H, F, alkyl; or R<sub>5</sub> and R<sub>7</sub> can be taken together to be oxo; R<sub>6</sub> = carboxy, alkoxy-carbonyl, amido, acyl, alkyl, OH, alkoxy; R<sub>9</sub> = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydropyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBT, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**

(non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT	<b>186392-40-5P</b>	186392-46-1P	186392-47-2P	186392-49-4P	
	186392-51-8P	186392-52-9P	186392-53-0P	186392-64-3P	186392-65-4P
	186392-70-1P	186429-64-1P	186429-91-4P	186430-03-5P	186430-23-9P
	186430-41-1P	186430-83-1P	186431-27-6P	186431-28-7P	186431-29-8P
	225929-30-6P	251446-20-5P	251446-21-6P	251446-22-7P	251446-23-8P
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	251446-29-4P	251446-30-7P	251446-31-8P	251446-32-9P	251446-33-0P
	251446-34-1P	251446-35-2P	332098-11-0P	332098-12-1P	332098-13-2P
	332098-14-3P	332098-15-4P	332098-16-5P	332098-17-6P	332098-18-7P
	332098-19-8P	332098-20-1P	332098-21-2P	332098-22-3P	332098-23-4P
	332098-24-5P	332098-25-6P	332098-26-7P	332098-27-8P	332098-28-9P
	332098-29-0P	332098-30-3P	332098-31-4P	332098-32-5P	332098-33-6P
	332098-34-7P	332098-35-8P	332098-36-9P	332098-37-0P	332098-38-1P
	332098-39-2P	332098-40-5P	332098-41-6P	332098-42-7P	332098-43-8P
	332098-44-9P	332098-45-0P	332098-46-1P	332098-47-2P	332098-48-3P
	332098-49-4P	332098-50-7P	332098-52-9P	332098-54-1P	332098-55-2P
	332098-57-4P	332098-59-6P	332098-61-0P	332098-63-2P	332098-65-4P
	362521-64-0P	362521-65-1P	362521-66-2P	362521-89-9P	362521-91-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L32 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:693054 HCAPLUS  
 DOCUMENT NUMBER: 135:247221  
 TITLE: Pharmaceutical compositions containing glycogen  
 phosphorylase inhibitors  
 INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen,  
 Dwayne Thomas; Lorenz, Douglas Alan; Nightingale,  
 James Alan Schriver  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: PCT Int. Appl., 142 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,  
 HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
 LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,  
 RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,  
 VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001053778	A1	20011220	US 2001-805828	20010314
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PRIORITY APPLN. INFO.: US 2000-189942P P 20000316

OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a glycogen phosphorylase inhibitor and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of glycogen phosphorylase inhibitor and concn.-enhancing polymer or a dispersion of glycogen phosphorylase inhibitor and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Heart, disease**  
 (diabetic cardiomyopathy; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)  
 IT **Heart, disease**  
 (ischemia; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)  
 IT **Diabetes mellitus**  
 (non-insulin-dependent; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)  
 IT Antitumor agents

Atherosclerosis  
 Cataract  
 Digestive tract  
 Dissolution rate  
 Drug bioavailability  
 Hypercholesterolemia  
 Hyperglycemia  
 Hypertension  
 Hypertriglyceridemia  
**Ischemia**  
 Solubility  
 Solvent effect

(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(inhibitors; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT 186392-40-5 186392-43-8 186392-51-8 186392-53-0  
 186392-63-2 186392-65-4 186429-91-4 186430-03-5 186430-23-9  
 186430-40-0 186430-57-9 186431-27-6 251446-20-5 251446-21-6  
 251446-32-9 332098-16-5 332098-17-6 361176-31-0

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

L32 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:554794 HCAPLUS

DOCUMENT NUMBER: 135:132447

TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethylamide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of

- diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.
- IT **Blood vessel, disease**  
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **Heart, disease**  
(diabetic cardiomyopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Cardiovascular system**  
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **Heart, disease**  
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Heart, disease**  
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Heart, disease**  
(ischemia; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 **186392-40-5** 186392-49-4 186392-65-4 186392-67-6 186392-70-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **9035-74-9, Glycogen phosphorylase**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

L32 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:566034 HCAPLUS

DOCUMENT NUMBER: 131:199699

TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia

INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 246 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943663	A1	19990902	WO 1999-IB206	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205
EP 1056729	A1	20001206	EP 1999-901083	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002504546	T2	20020212	JP 2000-533420	19990205
ZA 9901578	A	20000828	ZA 1999-1578	19990226
NO 2000004192	A	20000822	NO 2000-4192	20000822
PRIORITY APPLN. INFO.:			US 1998-76362P	P 19980227
			WO 1999-IB206	W 19990205
OTHER SOURCE(S):		MARPAT 131:199699		
AB	Guanidine derivs. ZCON:C(NH <sub>2</sub> ) <sub>2</sub> [I; Z = certain (un)substituted, diunsatd., diazoles and triazoles] and their pharmaceutically acceptable salts and/or prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical compns. contg. them. I are useful for the redn. of tissue damage resulting from tissue ischemia (no data). A large no. of compds. I and their intermediates were prepd. and/or specifically claimed. For instance, guanidine-HCl was converted to the free base, taken up in THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and the resultant guanidine deriv. was isolated and acidified with HCl in MeOH, to give title compd. II.HCl in 17% yield.			
REFERENCE COUNT:	6	THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		
IT	Brain, disease Heart, disease Intestine, disease Kidney, disease Liver, disease Lung, disease Muscle, disease Pancreas, disease Spleen (ischemia; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)			
IT	Ischemia (prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)			
IT	9028-31-3, Aldose reductase 9035-74-9, Glycogen phosphorylase RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study) (pharmaceuticals also contg. inhibitors of; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for			

treatment of ischemia)  
 IT 110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazineacetic acid **186392-40-5**  
 186392-43-8 186392-49-4 186392-53-0 186392-64-3 186392-65-4  
 186429-64-1 186429-78-7 186429-91-4 186430-03-5 186430-23-9  
 186430-41-1 186430-57-9 186431-27-6 225929-30-6  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceuticals contg.; prepn. of diazole and triazole guanidine  
 derivs. as NHE-1 inhibitors for treatment of ischemia)

L32 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:354425 HCAPLUS  
 DOCUMENT NUMBER: 131:9635  
 TITLE: Combination of an aldose reductase inhibitor and a  
 glycogen phosphorylase inhibitor  
 INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin,  
 Bernard; Treadway, Judith Lee  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: PCT Int. Appl., 119 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427
PRIORITY APPLN. INFO.:			US 1997-66365P	P 19971121
			WO 1998-IB1752	W 19981102

AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and glycogen phosphorylase inhibitors (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Acromegaly  
 Anti-infective agents  
 Anti-ischemic agents  
 Anticholesteremic agents  
 Antidiabetic agents  
 Antihypertensives  
 Antiobesity agents  
 Brain, disease  
 Cardiovascular agents  
 Drug delivery systems  
**Heart, disease**  
 Hypolipemic agents  
 Kidney, disease  
 Liver, disease  
 Lung, disease  
 Muscle, disease  
 Pancreas, disease  
 Pregnancy  
 Spleen, disease  
 (compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Diabetes mellitus**  
 (non-insulin-dependent; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Heart**  
 (surgery; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 110703-94-1 **186392-40-5** 186392-43-8 186392-49-4  
 186392-53-0 186392-64-3 186429-64-1 186429-78-7 186430-11-5  
 186430-23-9 186430-41-1 186430-52-4 186431-27-6 208830-24-4  
 208830-25-5 225929-30-6  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (compns. for **inhibitors** of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

L32 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:450920 HCAPLUS

DOCUMENT NUMBER: 129:189205

TITLE: Indole-2-carboxamide inhibitors of human liver glycogen phosphorylase

AUTHOR(S): Hoover, Dennis J.; Lefkowitz-Snow, Sheri; Burgess-Henry, Jana L.; Martin, William H.; Armento, Sandra J.; Stock, Ingrid A.; McPherson, R. Kirk; Genereux, Paul E.; Gibbs, E. Michael; Treadway, Judith L.

CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases  
 Medicinal Chemistry, Central Research Division, Pfizer Inc., Groton, CT, 06340, USA



SOURCE: Journal of Medicinal Chemistry (1998), 41(16),  
2934-2938  
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Indole-2-carboxamide derivs. (I; X = Cl, F, Br, H, OMe; R = Ph, cyclohexyl, H, F; Y = CONMe<sub>2</sub>, CONHMe, CO<sub>2</sub>Me, CO<sub>2</sub>H, CH<sub>2</sub>OH, CONH<sub>2</sub>, etc.) were prepd. I are potent inhibitors of human liver glycogen phosphorylase which are active in cells, and produce hypoglycemic activity on oral administration in a rodent model of type 2 diabetes. I [CP-320626; X = Cl, R = F, Y = CO(1-piperidin-4-ol)] produced oral activity at 10 mg/kg.

IT **Diabetes mellitus**  
(non-insulin-dependent; indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)

IT **9035-74-9**, Glycogen phosphorylase  
RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
(human liver; indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)

IT 17186-56-0P 78800-68-7P 109522-21-6P 111258-71-0P 111321-55-2P  
123665-42-9P 186392-10-9P 186392-11-0P 186392-12-1P 186392-13-2P  
186392-22-3P 186392-32-5P 186392-33-6P 186392-34-7P 186392-38-1P  
**186392-40-5P** 186392-56-3P 186429-59-4P 186429-60-7P  
186430-05-7P 186430-23-9P 186430-32-0P 186430-34-2P 186430-36-4P  
186430-37-5P 186430-39-7P 186430-44-4P 186431-50-5P 186431-51-6P  
186431-67-4P 186431-68-5P 186432-24-6P 186432-25-7P 186432-26-8P  
211677-10-0P 211677-11-1P 211677-12-2P 211677-13-3P 211677-14-4P  
211677-15-5P 211677-16-6P 211677-17-7P 211677-18-8P 211677-19-9P  
211677-20-2P 211677-21-3P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)

L32 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:388320 HCAPLUS

DOCUMENT NUMBER: 129:72196

TITLE: Use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia

INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 52 pp.  
CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		

AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204

PRIORITY APPLN. INFO.: US 1996-31584P P 19961205

OTHER SOURCE(S): MARPAT 129:72196

AB The use of a glycogen phosphorylase inhibitor for the manuf. of a medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal code, retina tissue, the vasculature or intestinal tissue. Said glycogen phosphorylase inhibitor is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH<sub>2</sub> or CH(C1-4 alkyl) when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6-, or 7-NO<sub>2</sub>, cyano, C1-4 alkyl or alkoxy, CH<sub>2</sub>F, CF<sub>2</sub>H, CF<sub>3</sub>; R<sub>2</sub> = H; R<sub>3</sub> = H, C1-5 alkyl; R<sub>4</sub> = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R<sub>5</sub> = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R<sub>7</sub> = H, F, C1-5 alkyl; or R<sub>5</sub> and R<sub>7</sub> are taken together to form oxo; R<sub>6</sub> = CO<sub>2</sub>H, C1-8 alkoxycarbonyl, (un)substituted CONH<sub>2</sub>, COR<sub>12</sub>; wherein R<sub>12</sub> = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thizolidin-3-yl, etc.], e.g. indolecarboxamide (II) which inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC<sub>50</sub> of 45 and 85 nM, resp.

IT **Blood vessel, disease**

Brain, disease

Intestine, disease

Intestine, disease

Kidney, disease

Liver, disease

Lung, disease

Nerve, disease

Pancreas, disease

Pancreas, disease

Spinal cord

(injury; use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from **ischemia** or hypoxia)

IT Animal tissue

Digestive tract

Hypoxia, animal

**Ischemia**

Spleen

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 186392-43-8 186392-46-1 186392-49-4

186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9

186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 186392-43-8 186392-46-1 186392-49-4

186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9

186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

L32 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:121995 HCAPLUS

DOCUMENT NUMBER: 128:252809

TITLE: Discovery of a human liver glycogen phosphorylase inhibitor that lowers blood glucose in vivo

AUTHOR(S): Martin, William H.; Hoover, Dennis J.; Armento, Sandra J.; Stock, Ingrid A.; Mcpherson, R. Kirk; Danley, Dennis E.; Stevenson, Ralph W.; Barrett, Eugene J.; Treadway, Judith L.

CORPORATE SOURCE: Central Research Division, Department of Exploratory Medicinal Biology, Pfizer, Inc, Groton, CT, 06340, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(4), 1776-1781  
CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An inhibitor of human liver glycogen phosphorylase a (HLGPa) has been identified and characterized in vitro and in vivo. This substance, [R-(R\*,S\*)]-5-chloro-N-[3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-1H-indole-2-carboxamide (CP-91149), inhibited HLGPa with an IC50 of 0.13 .mu.M in the presence of 7.5 mM glucose. CP-91149 resembles caffeine, a known allosteric phosphorylase inhibitor, in that it is 5- to 10-fold less potent in the absence of glucose. Further anal., however, suggests that CP-91149 and caffeine are kinetically distinct. Functionally, CP-91149 inhibited glucagon-stimulated glycogenolysis in isolated rat hepatocytes (P < 0.05 at 10-100 .mu.M) and in primary human hepatocytes (2.1 .mu.M IC50). In vivo, oral administration of CP-91149 to diabetic ob/ob mice at 25-50 mg/kg resulted in rapid (3 h) glucose lowering by 100-120 mg/dL (P < 0.001) without producing hypoglycemia. Further, CP-91149 treatment did not lower glucose levels in normoglycemic, nondiabetic mice. In ob/ob mice pretreated with 14C-glucose to label liver glycogen, CP-91149 administration reduced 14C-glycogen breakdown, confirming that glucose lowering resulted from inhibition of glycogenolysis in vivo. These findings support the use of CP-91149 in investigating glycogenolytic vs. gluconeogenic flux in hepatic glucose prodn., and they demonstrate that glycogenolysis inhibitors may be useful in the treatment of type 2 diabetes.

IT **Diabetes mellitus**  
(non-insulin-dependent; blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

IT **186392-40-5P**, CP 91149

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

=> FIL STNGUIDE

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FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Aug 30, 2002 (20020830/UP).

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L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR  
PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI  
L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)  
L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT  
OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR  
PKT OR DMA)/RL  
L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT  
OR DIABETES MELLITUS+NT,PFT/CT  
L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC  
CARDIOMYOPATHY"+PFT/CT  
L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/C  
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L7 20270 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOP  
ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT  
OR ISCHEMIA+NT,PFT/CT  
L8 9348 SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR  
"REPERFUSION (L) INJURY"+PFT/CT  
L9 335374 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6  
OR L7 OR L8)  
L11 1 SEA FILE=REGISTRY ABB=ON PLU=ON 186392-39-2/RN  
L18 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L11  
L25 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L18  
L31 2 SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR WO199639385/  
PN  
L33 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L25 NOT L31

*claim 2, 2nd compound  
pag #*

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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3  
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

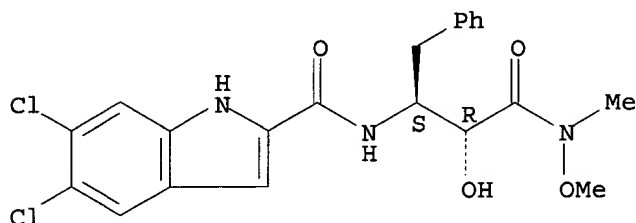
Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L11

L11 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
RN 186392-39-2 REGISTRY  
CN 1H-Indole-2-carboxamide, 5,6-dichloro-N-[(1S,2R)-2-hydroxy-3-  
(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Indole-2-carboxamide, 5,6-dichloro-N-[2-hydroxy-3-(methoxymethylamino)-

3-oxo-1-(phenylmethyl)propyl]-, [R-(R\*,S\*)]-  
 FS STEREOSEARCH  
 MF C21 H21 Cl2 N3 O4  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10  
 FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> D IBIB AB HIT L33

L33 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:554794 HCAPLUS  
 DOCUMENT NUMBER: 135:132447  
 TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for

*Hits in CAPLUS having  
key words & compound.*

treatment of diabetic cardiomyopathy  
 INVENTOR(S) : Treadway, Judith Lee  
 PATENT ASSIGNEE(S) : Pfizer Products Inc., USA  
 SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123
PRIORITY APPLN. INFO.:		US 2000-177770P P 20000124		
AB	Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.			
IT	<b>Blood vessel, disease</b> (diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)			
IT	<b>Heart, disease</b> (diabetic cardiomyopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of <b>diabetic cardiomyopathy</b> and other cardiovascular diseases)			
IT	<b>Cardiovascular system</b> (disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)			
IT	<b>Heart, disease</b> (failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of <b>diabetic cardiomyopathy</b> and other cardiovascular diseases)			
IT	<b>Heart, disease</b> (infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of <b>diabetic cardiomyopathy</b> and other cardiovascular diseases)			
IT	<b>Heart, disease</b> (ischemia; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of <b>diabetic cardiomyopathy</b> and other cardiovascular diseases)			
IT	56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2			

186392-39-2 186392-40-5 186392-49-4 186392-65-4  
186392-67-6 186392-70-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT 9035-74-9, Glycogen phosphorylase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 12:00:31 ON 05 SEP 2002

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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L34

L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR  
PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI

L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)

L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT  
OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR  
PKT OR DMA)/RL

L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT  
OR DIABETES MELLITUS+NT,PFT/CT

L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC  
CARDIOMYOPATHY"+PFT/CT

L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/C  
T

L7 20270 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOP  
ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT  
OR ISCHEMIA+NT,PFT/CT

L8 9348 SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR  
"REPERFUSION (L) INJURY"+PFT/CT

L9 335374 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6  
OR L7 OR L8)

L12 1 SEA FILE=REGISTRY ABB=ON PLU=ON 186392-43-8/RN *claim 2, 3rd compound*

L19 7 SEA FILE=HCAPLUS ABB=ON PLU=ON L12

L26 6 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L19

L31 2 SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR WO199639385/  
PN

L34 5 SEA FILE=HCAPLUS ABB=ON PLU=ON L26 NOT L31

=> FIL REG

FILE 'REGISTRY' ENTERED AT 12:02:03 ON 05 SEP 2002

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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3  
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

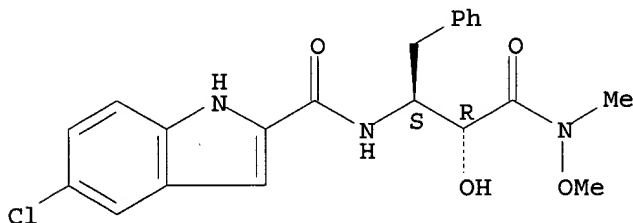
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L12

L12 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
RN 186392-43-8 REGISTRY  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]-, [R-(R\*,S\*)]-  
FS STEREOSEARCH  
MF C21 H22 Cl N3 O4  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

7 REFERENCES IN FILE CA (1967 TO DATE)  
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

FILE 'HCAPLUS' ENTERED AT 12:02:21 ON 05 SEP 2002  
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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10  
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L34 1-5

*Hits in CAPLUS*

L34 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2001:693054 HCAPLUS  
DOCUMENT NUMBER: 135:247221  
TITLE: Pharmaceutical compositions containing glycogen phosphorylase inhibitors  
INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 142 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053778	A1	20011220	US 2001-805828	20010314
PRIORITY APPLN. INFO.:			US 2000-189942P P 20000316	

OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a glycogen phosphorylase inhibitor and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of glycogen phosphorylase inhibitor and concn.-enhancing polymer or a dispersion of glycogen phosphorylase inhibitor and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel

chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Heart, disease**  
(diabetic cardiomyopathy; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **Heart, disease**  
(ischemia; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **Diabetes mellitus**  
(non-insulin-dependent; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT Antitumor agents  
Atherosclerosis  
Cataract  
Digestive tract  
Dissolution rate  
Drug bioavailability  
Hypercholesterolemia  
Hyperglycemia  
Hypertension  
Hypertriglyceridemia  
**Ischemia**  
Solubility  
Solvent effect  
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT **9035-74-9**, Glycogen phosphorylase  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(inhibitors; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT 186392-40-5 **186392-43-8** 186392-51-8 186392-53-0  
186392-63-2 186392-65-4 186429-91-4 186430-03-5 186430-23-9  
186430-40-0 186430-57-9 186431-27-6 251446-20-5 251446-21-6  
251446-32-9 332098-16-5 332098-17-6 361176-31-0  
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

L34 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:566034 HCAPLUS

DOCUMENT NUMBER: 131:199699

TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia

INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 246 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9943663      A1      19990902      WO 1999-IB206      19990205
W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
    DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
    KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
    MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
    TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
    TJ, TM
RW:  GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
    FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
    CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2321642      AA      19990902      CA 1999-2321642      19990205
AU 9920706      A1      19990915      AU 1999-20706      19990205
AU 739403       B2      20011011
BR 9908332      A        20001107      BR 1999-8332      19990205
EP 1056729      A1      20001206      EP 1999-901083      19990205
R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,
    SI, LT, LV, FI, RO
JP 2002504546   T2      20020212      JP 2000-533420      19990205
ZA 9901578      A        20000828      ZA 1999-1578      19990226
NO 2000004192   A        20000822      NO 2000-4192      20000822
PRIORITY APPLN. INFO.:      US 1998-76362P      P      19980227
                                WO 1999-IB206      W      19990205
OTHER SOURCE(S):      MARPAT 131:199699
AB  Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd.,
    diazoles and triazoles] and their pharmaceutically acceptable salts and/or
    prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger
    type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical
    compns. contg. them. I are useful for the redn. of tissue damage
    resulting from tissue ischemia (no data). A large no. of compds. I and
    their intermediates were prepd. and/or specifically claimed. For
    instance, guanidine-HCl was converted to the free base, taken up in
    THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-
    triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and
    the resultant guanidine deriv. was isolated and acidified with HCl in
    MeOH, to give title compd. II.HCl in 17% yield.
REFERENCE COUNT:      6      THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
IT  Brain, disease
    Heart, disease
    Intestine, disease
    Kidney, disease
    Liver, disease
    Lung, disease
    Muscle, disease
    Pancreas, disease
    Spleen
    (ischemia; prepn. of diazole and triazole guanidine derivs.
    as NHE-1 inhibitors for treatment of ischemia)
IT  Ischemia
    (prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors
    for treatment of ischemia)
IT  9028-31-3, Aldose reductase 9035-74-9, Glycogen phosphorylase
    RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL
    (Biological study)
    (pharmaceuticals also contg. inhibitors of; prepn. of diazole
    and triazole guanidine derivs. as NHE-1 inhibitors for
    treatment of ischemia)
IT  110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-
    benzothiazolyl]methyl]-1-phthalazineacetic acid 186392-40-5

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186392-43-8 186392-49-4 186392-53-0 186392-64-3  
 186392-65-4 186429-64-1 186429-78-7 186429-91-4 186430-03-5  
 186430-23-9 186430-41-1 186430-57-9 186431-27-6 225929-30-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceuticals contg.; prepn. of diazole and triazole guanidine  
 derivs. as NHE-1 inhibitors for treatment of ischemia)

L34 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:354425 HCAPLUS

DOCUMENT NUMBER: 131:9635

TITLE: Combination of an aldose reductase inhibitor and a  
 glycogen phosphorylase inhibitor

INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin,  
 Bernard; Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427
PRIORITY APPLN. INFO.:			US 1997-66365P	P 19971121
			WO 1998-IB1752	W 19981102

AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and glycogen phosphorylase inhibitors (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Acromegaly

Anti-infective agents  
 Anti-ischemic agents  
 Anticholesteremic agents  
 Antidiabetic agents  
 Antihypertensives  
 Antiobesity agents  
 Brain, disease  
 Cardiovascular agents  
 Drug delivery systems

**Heart, disease**

Hypolipemic agents  
 Kidney, disease  
 Liver, disease  
 Lung, disease  
 Muscle, disease  
 Pancreas, disease  
 Pregnancy  
 Spleen, disease

(compns. for inhibitors of aldose reductase and glycogen phosphorylase  
 for prevention and treatment of insulin resistant conditions in humans)

IT **Diabetes mellitus**

(non-insulin-dependent; compns. for inhibitors of aldose reductase and  
 glycogen phosphorylase for prevention and treatment of insulin  
 resistant conditions in humans)

IT **Heart**

(surgery; compns. for inhibitors of aldose reductase and glycogen  
 phosphorylase for prevention and treatment of insulin resistant  
 conditions in humans)

IT 110703-94-1 186392-40-5 **186392-43-8** 186392-49-4  
 186392-53-0 186392-64-3 186429-64-1 186429-78-7 186430-11-5  
 186430-23-9 186430-41-1 186430-52-4 186431-27-6 208830-24-4  
 208830-25-5 225929-30-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES  
 (Uses)

(compns. for inhibitors of aldose reductase and glycogen phosphorylase  
 for prevention and treatment of insulin resistant conditions in humans)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)

(compns. for **inhibitors** of aldose reductase and glycogen  
 phosphorylase for prevention and treatment of insulin resistant  
 conditions in humans)

L34 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:193899 HCAPLUS

DOCUMENT NUMBER: 130:227741

TITLE: Solid pharmaceutical dispersions with enhanced  
 bioavailability

INVENTOR(S): Curatolo, William John; Herbig, Scott Max;  
 Nightingale, James Alan Schriver

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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EP 901786	A2	19990317	EP 1998-305960	19980727
EP 901786	A3	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207896	A	19990217	CN 1998-116282	19980810
JP 11116502	A2	19990427	JP 1998-227328	19980811
JP 2984661	B2	19991129		
BR 9803144	A	20000111	BR 1998-3144	19980811
US 2002009494	A1	20020124	US 2001-770562	20010126

PRIORITY APPLN. INFO.: US 1997-55221P P 19970811  
US 1998-131019 B1 19980807

AB Spray dried solid dispersions comprising a sparingly sol. drug and hydroxypropyl Me cellulose acetate succinate (HPMCAS) provide increased aq. soly. and/or bioavailability in a use environment. Spray dried compns. were prepd. from HPMCAS and compds. such as ziprasidone, griseofulvin, nifedipine and phenytoin.

IT 9015-71-8, Corticotropin releasing hormone 9035-74-9, Glycogen phosphorylase 80619-02-9, 5-Lipoxygenase  
RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; solid pharmaceutical dispersions with enhanced bioavailability)

IT 57-41-0, Phenytoin 126-07-8, Griseofulvin 21829-25-4, Nifedipine 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 146939-27-7, Ziprasidone 175139-41-0 175140-00-8 **186392-43-8** 186392-65-4 221163-46-8  
RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (solid pharmaceutical dispersions with enhanced bioavailability)

L34 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 1998:388320 HCAPLUS  
DOCUMENT NUMBER: 129:72196  
TITLE: Use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia  
INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee  
PATENT ASSIGNEE(S): Pfizer Inc., USA  
SOURCE: Eur. Pat. Appl., 52 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		
AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204

PRIORITY APPLN. INFO.: US 1996-31584P P 19961205  
OTHER SOURCE(S): MARPAT 129:72196

AB The use of a glycogen phosphorylase inhibitor for the manuf. of a medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal cord, retina tissue, the vasculature or intestinal tissue. Said glycogen phosphorylase inhibitor is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH<sub>2</sub> or CH(C1-4 alkyl) when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6-, or 7-NO<sub>2</sub>, cyano, C1-4 alkyl or alkoxy, CH<sub>2</sub>F, CF<sub>2</sub>H, CF<sub>3</sub>; R<sub>2</sub> = H; R<sub>3</sub> = H, C1-5 alkyl; R<sub>4</sub> = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R<sub>5</sub> = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R<sub>7</sub> = H, F, C1-5 alkyl; or R<sub>5</sub> and R<sub>7</sub> are taken together to form oxo; R<sub>6</sub> = CO<sub>2</sub>H, C1-8 alkoxycarbonyl, (un)substituted CONH<sub>2</sub>, COR<sub>12</sub>; wherein R<sub>12</sub> = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thiazolidin-3-yl, etc.], e.g. indolecarboxamide (II) which inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC<sub>50</sub> of 45 and 85 nM, resp.

IT **Blood vessel, disease**

Brain, disease

Intestine, disease

Intestine, disease

Kidney, disease

Liver, disease

Lung, disease

Nerve, disease

Pancreas, disease

Pancreas, disease

Spinal cord

(injury; use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from **ischemia** or hypoxia)

IT Animal tissue

Digestive tract

Hypoxia, animal

**Ischemia**

Spleen

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 **186392-43-8** 186392-46-1 186392-49-4

186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9

186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 **186392-43-8** 186392-46-1 186392-49-4

186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9

186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

=> FIL STNGUIDE

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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L35

L1	6031	SEA FILE=HCAPLUS ABB=ON	PLU=ON	PHOSPHORYLASE+PFT/CT OR PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI
L2	465	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L1 (L) (INHIBIT? OR ANTAGONI?)
L3	153	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(ANTIDIABETIC AGENTS+NT,PFT/CT OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR PKT OR DMA)/RL
L4	47128	SEA FILE=HCAPLUS ABB=ON	PLU=ON	DIABETES INSIPIDUS+NT,PFT/CT OR DIABETES MELLITUS+NT,PFT/CT
L5	304	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"HEART, DISEASE (L) DIABETIC CARDIOMYOPATHY"+PFT/CT
L6	287453	SEA FILE=HCAPLUS ABB=ON	PLU=ON	CARDIOVASCULAR SYSTEM+NT,PFT/C T
L7	20270	SEA FILE=HCAPLUS ABB=ON	PLU=ON	"HEART, DISEASE (L) CARDIOMYOP ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT OR ISCHEMIA+NT,PFT/CT
L8	9348	SEA FILE=HCAPLUS ABB=ON	PLU=ON	REPERFUSION+PFT/CT OR "REPERFUSION (L) INJURY"+PFT/CT
L9	335374	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8)
L13	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	186392-49-4/RN
L20	7	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L13
L27	6	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L9 AND L20
L31	2	SEA FILE=HCAPLUS ABB=ON	PLU=ON	WO199639384/PN OR WO199639385/ PN
L35	5	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L27 NOT L31

*claim 2, 4th compound*

=> FIL REG

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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3  
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

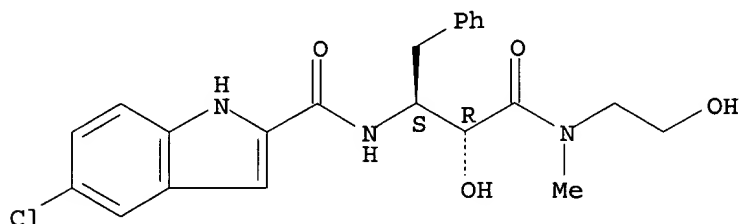
Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L13



L13 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS  
RN 186392-49-4 REGISTRY  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]-, [R-(R\*,S\*)]-  
FS STEREOSEARCH  
MF C22 H24 Cl N3 O4  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

7 REFERENCES IN FILE CA (1967 TO DATE)  
7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10  
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=&gt; D IBIB AB HIT L35 1-5

L35 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:709687 HCAPLUS

DOCUMENT NUMBER: 135:272869

TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 78 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319
PRIORITY APPLN. INFO.:			US 2000-191381P	P 20000322
OTHER SOURCE(S): MARPAT 135:272869				

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH<sub>2</sub>, CH-alkyl when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6- or 7-NO<sub>2</sub>, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R<sub>2</sub> = H; R<sub>3</sub> = H, alkyl; R<sub>4</sub> = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R<sub>5</sub> = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R<sub>7</sub> = H, F, alkyl; or R<sub>5</sub> and R<sub>7</sub> can be taken together to be oxo; R<sub>6</sub> = carboxy, alkoxy-carbonyl, amido, acyl, alkyl, OH, alkoxy; R<sub>9</sub> = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBT, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**  
(non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT

186392-40-5P	186392-46-1P	186392-47-2P	186392-49-4P	
186392-51-8P	186392-52-9P	186392-53-0P	186392-64-3P	186392-65-4P
186392-70-1P	186429-64-1P	186429-91-4P	186430-03-5P	186430-23-9P
186430-41-1P	186430-83-1P	186431-27-6P	186431-28-7P	186431-29-8P
225929-30-6P	251446-20-5P	251446-21-6P	251446-22-7P	251446-23-8P
251446-24-9P	251446-25-0P	251446-26-1P	251446-27-2P	251446-28-3P
251446-29-4P	251446-30-7P	251446-31-8P	251446-32-9P	251446-33-0P
251446-34-1P	251446-35-2P	332098-11-0P	332098-12-1P	332098-13-2P
332098-14-3P	332098-15-4P	332098-16-5P	332098-17-6P	332098-18-7P
332098-19-8P	332098-20-1P	332098-21-2P	332098-22-3P	332098-23-4P
332098-24-5P	332098-25-6P	332098-26-7P	332098-27-8P	332098-28-9P
332098-29-0P	332098-30-3P	332098-31-4P	332098-32-5P	332098-33-6P
332098-34-7P	332098-35-8P	332098-36-9P	332098-37-0P	332098-38-1P
332098-39-2P	332098-40-5P	332098-41-6P	332098-42-7P	332098-43-8P
332098-44-9P	332098-45-0P	332098-46-1P	332098-47-2P	332098-48-3P
332098-49-4P	332098-50-7P	332098-52-9P	332098-54-1P	332098-55-2P

332098-57-4P 332098-59-6P 332098-61-0P 332098-63-2P 332098-65-4P  
 362521-64-0P 362521-65-1P 362521-66-2P 362521-89-9P 362521-91-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors  
 for treatment of type 2 diabetes)

L35 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:554794 HCAPLUS

DOCUMENT NUMBER: 135:132447

TITLE: Chloroindolephenylethylamide analogs and their  
 prodrugs as glycogen phosphorylase inhibitors for  
 treatment of diabetic cardiomyopathy

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-  
 carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-  
 phenylethyl]amide, etc., and their prodrugs are claimed as glycogen  
 phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The  
 title compds. can also combine with insulin, insulin analogs (biguanides),  
 .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma.  
 agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors,  
 .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity  
 agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose  
 reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid  
 receptor antagonists, and/or thyroid hormone analogs for treatment of  
 diabetes, cardiovascular diseases, heart ischemia, congestive heart  
 failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**

(diabetic angiopathy; chloroindolephenylethylamide analogs and their  
 prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic  
 cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**

(diabetic cardiomyopathy;  
 chloroindolephenylethylamide analogs and their prodrugs as glycogen  
 phosphorylase inhibitors for treatment of **diabetic**  
**cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**

(disease; chloroindolephenylethylamide analogs and their prodrugs as  
 glycogen phosphorylase inhibitors for treatment of diabetic  
 cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**

(failure; chloroindolephenylethylamide analogs and their prodrugs as  
 glycogen phosphorylase inhibitors for treatment of **diabetic**

**cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**  
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**  
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 **186392-49-4** 186392-65-4 186392-67-6 186392-70-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **9035-74-9**, Glycogen phosphorylase  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

L35 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:566034 HCAPLUS

DOCUMENT NUMBER: 131:199699

TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia

INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 246 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943663	A1	19990902	WO 1999-IB206	19990205
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205

EP 1056729            A1    20001206            EP 1999-901083    19990205  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,  
 SI, LT, LV, FI, RO  
 JP 2002504546        T2    20020212            JP 2000-533420    19990205  
 ZA 9901578            A    20000828            ZA 1999-1578       19990226  
 NO 2000004192        A    20000822            NO 2000-4192       20000822  
 PRIORITY APPLN. INFO.:            US 1998-76362P    P    19980227  
    WO 1999-IB206       W    19990205

OTHER SOURCE(S):            MARPAT 131:199699

AB    Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd.,  
 diazoles and triazoles] and their pharmaceutically acceptable salts and/or  
 prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger  
 type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical  
 compns. contg. them. I are useful for the redn. of tissue damage  
 resulting from tissue ischemia (no data). A large no. of compds. I and  
 their intermediates were prepd. and/or specifically claimed. For  
 instance, guanidine-HCl was converted to the free base, taken up in  
 THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-  
 triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and  
 the resultant guanidine deriv. was isolated and acidified with HCl in  
 MeOH, to give title compd. II.HCl in 17% yield.

REFERENCE COUNT:            6            THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS  
    RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT    Brain, disease  
       **Heart, disease**  
       Intestine, disease  
       Kidney, disease  
       Liver, disease  
       Lung, disease  
       Muscle, disease  
       Pancreas, disease  
       Spleen  
       (ischemia; prepn. of diazole and triazole guanidine derivs.  
       as NHE-1 inhibitors for treatment of ischemia)  
 IT    **Ischemia**  
       (prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors  
       for treatment of ischemia)  
 IT    9028-31-3, Aldose reductase 9035-74-9, Glycogen phosphorylase  
       RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL  
       (Biological study)  
       (pharmaceuticals also contg. inhibitors of; prepn. of diazole  
       and triazole guanidine derivs. as NHE-1 inhibitors for  
       treatment of ischemia)  
 IT    110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-  
       benzothiazolyl]methyl]-1-phthalazineacetic acid    186392-40-5  
       186392-43-8 **186392-49-4**    186392-53-0    186392-64-3  
       186392-65-4    186429-64-1    186429-78-7    186429-91-4    186430-03-5  
       186430-23-9    186430-41-1    186430-57-9    186431-27-6    225929-30-6  
       RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
       (pharmaceuticals contg.; prepn. of diazole and triazole guanidine  
       derivs. as NHE-1 inhibitors for treatment of ischemia)

L35 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:            1999:354425 HCAPLUS

DOCUMENT NUMBER:            131:9635

TITLE:                        Combination of an aldose reductase inhibitor and a  
    glycogen phosphorylase inhibitor

INVENTOR(S):                Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin,  
    Bernard; Treadway, Judith Lee

PATENT ASSIGNEE(S):        Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 119 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427
PRIORITY APPLN. INFO.:			US 1997-66365P	P 19971121
			WO 1998-IB1752	W 19981102
AB	Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and glycogen phosphorylase inhibitors (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as diabetes, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.			
REFERENCE COUNT:	3	THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT		

IT Acromegaly  
 Anti-infective agents  
 Anti-ischemic agents  
 Anticholesteremic agents  
 Antidiabetic agents  
 Antihypertensives  
 Antiobesity agents  
 Brain, disease  
 Cardiovascular agents  
 Drug delivery systems  
 Heart, disease  
 Hypolipemic agents  
 Kidney, disease  
 Liver, disease  
 Lung, disease  
 Muscle, disease

Pancreas, disease

Pregnancy

Spleen, disease

(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Diabetes mellitus**

(non-insulin-dependent; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT **Heart**

(surgery; compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 110703-94-1 186392-40-5 186392-43-8 **186392-49-4**

186392-53-0 186392-64-3 186429-64-1 186429-78-7 186430-11-5

186430-23-9 186430-41-1 186430-52-4 186431-27-6 208830-24-4

208830-25-5 225929-30-6

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compns. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(compns. for **inhibitors** of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

L35 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:388320 HCAPLUS

DOCUMENT NUMBER: 129:72196

TITLE: Use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia

INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 52 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		
AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204

PRIORITY APPLN. INFO.: US 1996-31584P P 19961205

OTHER SOURCE(S): MARPAT 129:72196

AB The use of a glycogen phosphorylase inhibitor for the manuf. of a

medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal cord, retina tissue, the vasculature or intestinal tissue. Said glycogen phosphorylase inhibitor is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH<sub>2</sub> or CH(C1-4 alkyl) when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6-, or 7-NO<sub>2</sub>, cyano, C1-4 alkyl or alkoxy, CH<sub>2</sub>F, CF<sub>2</sub>H, CF<sub>3</sub>; R<sub>2</sub> = H; R<sub>3</sub> = H, C1-5 alkyl; R<sub>4</sub> = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R<sub>5</sub> = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R<sub>7</sub> = H, F, C1-5 alkyl; or R<sub>5</sub> and R<sub>7</sub> are taken together to form oxo; R<sub>6</sub> = CO<sub>2</sub>H, C1-8 alkoxycarbonyl, (un)substituted CONH<sub>2</sub>, COR<sub>12</sub>; wherein R<sub>12</sub> = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thiazolidin-3-yl, etc.], e.g. indolecarboxamide (II) which inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC<sub>50</sub> of 45 and 85 nM, resp.

IT **Blood vessel, disease**

Brain, disease

Intestine, disease

Intestine, disease

Kidney, disease

Liver, disease

Lung, disease

Nerve, disease

Pancreas, disease

Pancreas, disease

Spinal cord

(injury; use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from **ischemia** or hypoxia)

IT **Animal tissue**

Digestive tract

Hypoxia, animal

**Ischemia**

Spleen

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 186392-43-8 186392-46-1 **186392-49-4**

186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9

186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

IT 186392-40-5 186392-43-8 186392-46-1 **186392-49-4**

186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9

186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

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FILE 'STNGUIDE' ENTERED AT 12:07:02 ON 05 SEP 2002



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FILE CONTAINS CURRENT INFORMATION.  
LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L36

L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR  
PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI  
L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)  
L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT  
OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR  
PKT OR DMA)/RL  
L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT  
OR DIABETES MELLITUS+NT,PFT/CT  
L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC  
CARDIOMYOPATHY"+PFT/CT  
L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/C  
T  
L7 20270 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOP  
ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT  
OR ISCHEMIA+NT,PFT/CT  
L8 9348 SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR  
"REPERFUSION (L) INJURY"+PFT/CT  
L9 335374 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6  
OR L7 OR L8)  
L14 1 SEA FILE=REGISTRY ABB=ON PLU=ON 186392-65-4/RN *dr 2, 5th compound*  
L21 11 SEA FILE=HCAPLUS ABB=ON PLU=ON L14  
L28 10 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L21  
L31 2 SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR WO199639385/  
PN  
L36 9 SEA FILE=HCAPLUS ABB=ON PLU=ON L28 NOT L31

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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3  
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

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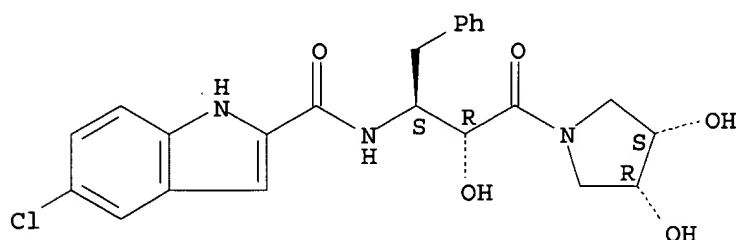
Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L14

L14 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 186392-65-4 REGISTRY  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-, [R-[R\*,S\*-(cis)]]-  
OTHER NAMES:  
CN Ingliforib  
FS STEREOSEARCH  
MF C23 H24 Cl N3 O5  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

11 REFERENCES IN FILE CA (1967 TO DATE)  
11 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10  
FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L36 1-9

L36 ANSWER 1 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:936092 HCAPLUS

DOCUMENT NUMBER: 136:53752

TITLE: Synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors

INVENTOR(S): Mylari, Banavara L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 41 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2001056095	A1	20011227	US 2001-782798	20010213
PRIORITY APPLN. INFO.:				US 2000-183004P	P 20000216
AB	Mono-, di- and triethanolamine salts of [4-Oxo-(5-trifluoromethylbenzothiazol-2-ylmethyl)-3,4-dihydrophthalazin-1-yl]acetic acid (zopolrestat; I) were prepd. E.g., a soln. of I in acetone was added to ethanolamine (10 mol equiv, room temp., 1 h) which afforded, after purifn., the ethanolamine salt in 95% yield, m.p. 119 - 121.degree.C. Ethanolamine salts of I are used alone or with NHE-1 inhibitors (e.g. II), selective serotonin reuptake inhibitors (SSRIs, e.g. fluoxetine), glycogen phosphorylase inhibitors (GPIs), sorbitol dehydrogenase inhibitors (SDIs) and antihypertensive agents for treating diabetic complications.				
IT	<b>Diabetes insipidus</b> (complications from)				
IT	<b>Heart, disease</b> (diabetic cardiomyopathy; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)				
IT	<b>Heart, disease</b> (infarction; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)				
IT	<b>Blood vessel, disease</b> (microangiopathy; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)				
IT	54910-89-3, Fluoxetine 79559-97-0, Sertraline hydrochloride 79617-96-2, Sertraline 106650-56-0, Sibutramine 186392-65-4 241800-98-6 241801-81-0, [5-Isopropyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241801-83-2, [5-Propyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241801-85-4, [1-(2-Chlorophenyl)-5-methyl-1H-pyrazole-4-carbonyl]guanidine 241801-86-5, [5-Methyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine 241801-87-6, (5-Ethyl-1-phenyl-1H-pyrazole-4-carbonyl)guanidine 241801-88-7, [5-Cyclopropyl-1-(2-trifluoromethylphenyl)-1H-pyrazole-4-carbonyl]guanidine 241801-89-8, (5-Cyclopropyl-1-phenyl-1H-pyrazole-4-carbonyl)guanidine 241801-90-1, [5-Cyclopropyl-1-(2,6-dichlorophenyl)-1H-pyrazole-4-carbonyl]guanidine 241801-93-4, [5-Cyclopropyl-1-(quinolin-8-yl)-1H-pyrazole-4-carbonyl]guanidine 241802-04-0, [1-(2-Chloro-4-methylsulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-05-1, [1-(2-Chlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine				

241802-06-2, [1-(2-Trifluoromethyl-4-fluorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-07-3, [1-(2-Bromophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-08-4, [1-(2-Fluorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-09-5, [1-(2-Chloro-5-methoxyphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-10-8, [1-(2-Chloro-4-methylaminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-11-9, [1-(2,5-Dichlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-12-0, [1-(2,3-Dichlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-13-1, [1-(2-Chloro-5-aminocarbonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-14-2, [1-(2-Chloro-5-aminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-15-3, [1-(2-Fluoro-6-trifluoromethylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-16-4, [1-(2-Chloro-5-methylsulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-17-5, [1-(2-Chloro-5-dimethylaminosulfonylphenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-18-6, [1-(2-Trifluoromethyl-4-chlorophenyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-19-7, [1-(8-Bromoquinolin-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-20-0, [1-(6-Chloroquinolin-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-21-1, [1-(Indazol-7-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-22-2, [1-(Benzimidazol-5-yl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-23-3, [1-(1-Isoquinolyl)-5-cyclopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-24-4, [5-Cyclopropyl-1-(4-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241802-25-5, [1-(Indazol-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-26-6, [1-(Indazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-27-7, [1-(Benzimidazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-28-8, [1-(1-Methylbenzimidazol-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-29-9, [1-(5-Quinoliny)-5-n-propyl-1H-pyrazole-4-carbonyl]guanidine 241802-30-2, [1-(5-Quinoliny)-5-isopropyl-1H-pyrazole-4-carbonyl]guanidine 241802-31-3, [5-Ethyl-1-(6-quinolinyl)-1H-pyrazole-4-carbonyl]guanidine 241802-32-4, [1-(2-Methylbenzimidazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-33-5, [1-(1,4-Benzodioxan-6-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-34-6, [1-(Benzotriazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-35-7, [1-(3-Chloroindazol-5-yl)-5-ethyl-1H-pyrazole-4-carbonyl]guanidine 241802-36-8, [1-(5-Quinoliny)-5-butyl-1H-pyrazole-4-carbonyl]guanidine 300548-76-9, 1R-[4-[1'-(2-(1R)-Hydroxyethyl)pyrimidin-4-yl]-[4,4']bipiperidinyl-1-yl]pyrimidin-2-yl]ethanol 300548-89-4 300548-90-7 300548-92-9, 1R-[4-(2-Hydroxymethyl-6-methylpyrimidin-4-yl)-3S-methylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300548-93-0 300548-99-6 300549-00-2, 1R-[4-[4-(4,6-Dimethylpyrimidin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-02-4, 1R-[4-[4-(4-Hydroxymethyl-6-methylpyrimidin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-03-5, 1R-[4-[4-(2,6-Dimethylpyrimidin-4-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-05-7, 1R-[4-[4-(2-Hydroxymethyl-6-methylpyrimidin-4-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-16-0, 1R-[4-[4-(2-Hydroxymethylpyrimidin-4-yl)-3S-methylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300549-28-4 300549-30-8 300549-32-0 300549-34-2 300549-50-2 300549-51-3 300549-53-5 300549-58-0, 1R-[4-[4-(4-Hydroxymethyl-6-methylpyrimidin-2-yl)-3S-methylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300550-38-3 300550-60-1 300550-69-0 300551-01-3, 1R-[4-[2R,6S-Dimethyl-4-[2-(4-methylimidazol-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-03-5, 1R-[4-[4-[2-(2,4-Dimethylimidazol-1-yl)pyrimidin-4-yl]-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-04-6 300551-11-5,

1R-[4-[2R,6S-Dimethyl-4-[2-(4-methylpiperazin-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-12-6,  
 1R-[4-[2R,6S-Dimethyl-4-(2-morpholin-4-ylpyrimidin-4-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-17-1, 1R-[4-[3R,5S-Dimethyl-4-[2-(4-methylpiperazin-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-19-3, 1R-[4-[4-[2-(4-Ethylpiperazin-1-yl)pyrimidin-4-yl]-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-20-6,  
 1R-[4-[4-[2-(4-Isopropylpiperazin-1-yl)pyrimidin-4-yl]-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-21-7,  
 1R-[4-[2R,6S-Dimethyl-4-(4-morpholin-4-yl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-22-8, 1R-[4-[4-(4-Methoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-23-9, 1R-[4-[4-(4,6-Dimethoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-24-0,  
 1R-[4-[2R,6S-Dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-28-4, 1R-[4-[3R,5S-Dimethyl-4-[4-methyl-6-(4-methylpiperazin-1-yl)-[1,3,5]triazin-2-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-29-5, 1R-[4-[2R,6S-Dimethyl-4-(4-methyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-30-8,  
 1R-[4-[4-(4,6-Dimethoxy-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-31-9, 1R-[4-[4-(4-Ethoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-32-0, 1R-[4-[4-(4-Isopropoxy-6-methyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-33-1,  
 1R-[4-[3R,5S-Dimethyl-4-(4-phenyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-42-2, 1R-[4-[4-(4-Cyclopropyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-43-3 300551-45-5, 1R-[4-[4-(4-Hydroxymethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-48-8, 1R-[4-[4-(4-Hydroxymethyl-6-phenyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-49-9,  
 1R-[4-[4-(4,6-Dimethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-50-2, 1R-[4-[4-(4,6-Dimethyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-52-4, 1R-[4-[3R,5S-Dimethyl-4-(4-methyl-6-phenyl-[1,3,5]triazin-2-yl)piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-87-5 300551-88-6  
 300551-89-7 300551-90-0 300551-91-1 300551-92-2 300551-94-4  
 300551-95-5 300551-96-6, 1R-[4-[3R,5S-Dimethyl-4-[2-(4-methylimidazol-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-97-7,  
 1R-[4-[3R,5S-Dimethyl-4-[2-(2-methylimidazol-1-yl)pyrimidin-4-yl]piperazin-1-yl]pyrimidin-2-yl]ethanol 300551-98-8, 1R-[4-[4-[2-(2,4-Dimethylimidazol-1-yl)pyrimidin-4-yl]-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300551-99-9, 1R-[4-[4-(4-Isopropoxy-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-00-5, 1R-[4-[4-(4-Isopropyl-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-02-7,  
 1R-[4-[4-(4-Ethyl-6-methoxy-[1,3,5]triazin-2-yl)-3R,5S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-03-8, 1R-[4-[4-[2-(4-Ethylpiperazin-1-yl)pyrimidin-4-yl]-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-04-9, 1R-[4-[4-(4-Methoxy-6-methoxymethyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-06-1,  
 1R-[4-[4-(4-Methoxy-6-methyl-[1,3,5]triazin-2-yl)-2R,6S-dimethylpiperazin-1-yl]pyrimidin-2-yl]ethanol 300552-07-2 382142-96-3 382143-00-2  
 382143-43-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(combination pharmaceutical; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

L36 ANSWER 2 OF 9 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2001:709687 HCAPLUS  
 DOCUMENT NUMBER: 135:272869  
 TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes  
 INVENTOR(S): Treadway, Judith Lee  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: Eur. Pat. Appl., 78 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319
PRIORITY APPLN. INFO.:			US 2000-191381P	P 20000322
OTHER SOURCE(S): MARPAT 135:272869				

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH<sub>2</sub>, CH-alkyl when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6- or 7-NO<sub>2</sub>, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R<sub>2</sub> = H; R<sub>3</sub> = H, alkyl; R<sub>4</sub> = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R<sub>5</sub> = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R<sub>7</sub> = H, F, alkyl; or R<sub>5</sub> and R<sub>7</sub> can be taken together to be oxo; R<sub>6</sub> = carboxy, alkoxy-carbonyl, amido, acyl, alkyl, OH, alkoxy; R<sub>9</sub> = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prep'd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **Diabetes mellitus**  
 (non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT 186392-40-5P	186392-46-1P	186392-47-2P	186392-49-4P	186392-51-8P
186392-52-9P	186392-53-0P	186392-64-3P	<b>186392-65-4P</b>	
186392-70-1P	186429-64-1P	186429-91-4P	186430-03-5P	186430-23-9P
186430-41-1P	186430-83-1P	186431-27-6P	186431-28-7P	186431-29-8P
225929-30-6P	251446-20-5P	251446-21-6P	251446-22-7P	251446-23-8P
251446-24-9P	251446-25-0P	251446-26-1P	251446-27-2P	251446-28-3P
251446-29-4P	251446-30-7P	251446-31-8P	251446-32-9P	251446-33-0P
251446-34-1P	251446-35-2P	332098-11-0P	332098-12-1P	332098-13-2P
332098-14-3P	332098-15-4P	332098-16-5P	332098-17-6P	332098-18-7P
332098-19-8P	332098-20-1P	332098-21-2P	332098-22-3P	332098-23-4P
332098-24-5P	332098-25-6P	332098-26-7P	332098-27-8P	332098-28-9P
332098-29-0P	332098-30-3P	332098-31-4P	332098-32-5P	332098-33-6P
332098-34-7P	332098-35-8P	332098-36-9P	332098-37-0P	332098-38-1P
332098-39-2P	332098-40-5P	332098-41-6P	332098-42-7P	332098-43-8P
332098-44-9P	332098-45-0P	332098-46-1P	332098-47-2P	332098-48-3P
332098-49-4P	332098-50-7P	332098-52-9P	332098-54-1P	332098-55-2P
332098-57-4P	332098-59-6P	332098-61-0P	332098-63-2P	332098-65-4P
362521-64-0P	362521-65-1P	362521-66-2P	362521-89-9P	362521-91-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L36 ANSWER 3 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:693088 HCAPLUS  
DOCUMENT NUMBER: 135:262225  
TITLE: Glycogen phosphorylase inhibitor compositions  
INVENTOR(S): Babcock, Walter C.; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Macri, Christopher A.; Nightingale, James Alan Schriver; Shanker, Ravi Mysore; Hancock, Bruno Caspar; Crew, Marshall D.  
PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
SOURCE: PCT Int. Appl., 116 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068092	A2	20010920	WO 2001-IB389	20010316
WO 2001068092	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053791	A1	20011220	US 2001-808559	20010314

PRIORITY APPLN. INFO.: US 2000-190125P P 20000316

AB Pharmaceutical compns. of a particularly effective sparingly sol. glycogen phosphorylase inhibitor are disclosed. Thus, an amorphous solid dispersion contg. 25% a drug and 75% polymer was made by first mixing the drug in acetone together with a finely powd. HPMCAS to form a soln. The soln. comprised 1.25% drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray via a 2-fluid external mix spray nozzle at 2.6 bar at a 175 to 180 g/min feed rate into a stainless steel chamber of a NIRO XP spray drier, maintained at a temp. of 180.degree. at the inlet and 69.degree. at the outlet.

IT 186392-65-4

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(glycogen phosphorylase inhibitor compns.)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; glycogen phosphorylase inhibitor compns.)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; glycogen phosphorylase inhibitor compns.)

L36 ANSWER 4 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:693054 HCAPLUS  
 DOCUMENT NUMBER: 135:247221  
 TITLE: Pharmaceutical compositions containing glycogen phosphorylase inhibitors  
 INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: PCT Int. Appl., 142 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

US 2001053778	A1	20011220	US 2001-805828	20010314
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PRIORITY APPLN. INFO.: US 2000-189942P P 20000316

OTHER SOURCE(S): MARPAT 135:247221

AB Pharmaceutical compns. comprise a glycogen phosphorylase inhibitor and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of glycogen phosphorylase inhibitor and concn.-enhancing polymer or a dispersion of glycogen phosphorylase inhibitor and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT **Heart, disease**  
 (diabetic cardiomyopathy; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)  
 IT **Heart, disease**  
 (ischemia; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)  
 IT **Diabetes mellitus**  
 (non-insulin-dependent; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)  
 IT Antitumor agents  
 Atherosclerosis  
 Cataract



Digestive tract  
 Dissolution rate  
 Drug bioavailability  
 Hypercholesterolemia  
 Hyperglycemia  
 Hypertension  
 Hypertriglyceridemia

**Ischemia**

Solubility  
 Solvent effect

(pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL  
 (Biological study)

(inhibitors; pharmaceutical compns. contg. glycogen  
 phosphorylase inhibitors)

IT 186392-40-5 186392-43-8 186392-51-8 186392-53-0 186392-63-2  
 186392-65-4 186429-91-4 186430-03-5 186430-23-9  
 186430-40-0 186430-57-9 186431-27-6 251446-20-5 251446-21-6  
 251446-32-9 332098-16-5 332098-17-6 361176-31-0

RL: BPR (Biological process); BSU (Biological study, unclassified); THU  
 (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (pharmaceutical compns. contg. glycogen phosphorylase inhibitors)

L36 ANSWER 5 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:554794 HCAPLUS

DOCUMENT NUMBER: 135:132447

TITLE: Chloroindolephenylethylamide analogs and their  
 prodrugs as glycogen phosphorylase inhibitors for  
 treatment of diabetic cardiomyopathy

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-  
 carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-  
 phenylethyl]amide, etc., and their prodrugs are claimed as glycogen  
 phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The  
 title compds. can also combine with insulin, insulin analogs (biguanides),  
 .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma.  
 agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors,  
 .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity  
 agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose  
 reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid  
 receptor antagonists, and/or thyroid hormone analogs for treatment of  
 diabetes, cardiovascular diseases, heart ischemia, congestive heart  
 failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

- IT **Blood vessel, disease**  
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **Heart, disease**  
(diabetic cardiomyopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Cardiovascular system**  
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **Heart, disease**  
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Heart, disease**  
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Heart, disease**  
(ischemia; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 186392-49-4 **186392-65-4** 186392-67-6 186392-70-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **9035-74-9**, Glycogen phosphorylase  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

L36 ANSWER 6 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:489208 HCAPLUS

DOCUMENT NUMBER: 135:97443

TITLE: Pharmaceutical compositions containing polymer for enhanced drug concentrations

INVENTOR(S): Babcock, Walter Christian; Curatolo, William John; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver; Shanker, Ravi Mysore

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 85 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001047495	A1	20010705	WO 2000-IB1787	20001201
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002006443	A1	20020117	US 2000-742785	20001220

## PRIORITY APPLN. INFO.:

US 1999-171841P P 19991223

AB A drug in a soly.-improved form is combined with a concn.-enhancing polymer, i.e., a cellulosic or non-cellulosic polymer, in a sufficient amt. so that the combination provides substantially enhanced drug concn. in a use environment,, such as digestive tract, s.c. space, vagina, lung, blood vessels, and muscle relative to a control comprising the same amt. of the same soly.-improved form of drug without the concn.-enhancing polymer. For example, the soly. of sertraline-HCl was increased in presence of citric acid, giving a soly.-improvement factor of 9.3. Thus, citric acid is an excellent solubilizing agent for sertraline-HCl. A soln. was prepd. contg. 1000 .mu.g/mL sertraline-HCl, 500 .mu.g/mL citric acid, and 1000 .mu.g/mL hydroxypropyl Me cellulose acetate succinate (HPMCAS) in phosphate buffer. (pH 7.9). Addn. of the concn.-enhancing polymer HPMCAS resulted in a max. concn. that was 1.7-fold that of control contg. no polymer.

REFERENCE COUNT:

4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT

**Artery**

Crystallization

Digestive tract

Dissolution rate

Drug delivery systems

Lung

Muscle

Polyelectrolytes

Solubility

Solubilization

Solubilizers

Vagina

**Vein**

(pharmaceutical compns. contg. polymer for enhanced drug concns.)

IT

9004-38-0, Cellulose acetate phthalate 9004-58-4, Hydroxyethyl ethyl cellulose 9004-63-1, Hydroxyethyl cellulose acetate 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 9032-42-2, Hydroxyethyl methyl cellulose 9050-31-1, Hydroxypropyl methyl cellulose phthalate 52907-01-4, Cellulose acetate trimellitate 54391-89-8, Cellulose acetate terephthalate 58858-21-2, Hydroxypropyl methyl cellulose acetate 67165-96-2, Hydroxypropyl methyl cellulose acetate phthalate 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 79559-97-0, Sertraline hydrochloride 89233-51-2, Cellulose propionate phthalate 167077-74-9, Cellulose propionate trimellitate 167077-75-0, Cellulose butyrate trimellitate 185021-64-1, Ziprasidone mesylate 186392-65-4 188979-58-0 219736-80-8 248594-19-6 249296-43-3 288141-80-0, Methyl cellulose acetate phthalate 288156-14-9, Hydroxypropyl methyl cellulose acetate trimellitate 288307-50-6, Hydroxypropyl cellulose butyrate phthalate 288307-51-7, Cellulose acetate isophthalate

288372-69-0, Ethyl phthalic acid cellulose acetate 288372-70-3,  
 Hydroxypropyl cellulose acetate phthalate succinate 288372-71-4, Methyl  
 cellulose acetate trimellitate 288372-72-5, Ethyl cellulose acetate  
 trimellitate 288372-73-6, Hydroxypropyl cellulose acetate trimellitate  
 288372-74-7, Hydroxypropyl cellulose acetate trimellitate succinate  
 288372-75-8, Cellulose acetate pyridinedicarboxylate 288372-76-9  
 288372-77-0, 288372-80-5, Ethyl nicotinic acid cellulose acetate  
 288372-81-6, Ethyl picolinic acid cellulose acetate 348078-72-8  
 348078-73-9

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic  
 use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (pharmaceutical compns. contg. polymer for enhanced drug concns.)

L36 ANSWER 7 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:573515 HCAPLUS

DOCUMENT NUMBER: 133:182970

TITLE: Matrix controlled release device for a low-solubility  
 drug

INVENTOR(S): Appel, Leah Elizabeth; Friesen, Dwayne Thomas;  
 Curatolo, William John; Nightingale, James Alan  
 Schriver; Thombre, Avinash Govind

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 26 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1027887	A2	20000816	EP 2000-300546	20000126
EP 1027887	A3	20010228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000229888	A2	20000822	JP 2000-33446	20000210
BR 2000000359	A	20010814	BR 2000-359	20000210

PRIORITY APPLN. INFO.: US 1999-119400P P 19990210

AB Disclosed are a controlled release dosage form for a low soly. drug that  
 is a spray-dried or spray-coated amorphous solid dispersion of the drug in  
 an ionizable cellulosic polymer matrix that is in turn incorporated into a  
 secondary erodible polymeric matrix and a method of treating a disease or  
 disorder comprising administering such a dosage form. A batch of solid  
 dispersion was prepd. by spray-drying a soln. contg. drug  
 5-chloro-1H-indole-2-carboxylic acid [(1S-benzyl-3-(3R,4S)-  
 dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxypropyl]amide (water soly. 80  
 .mu.g/mL) in acetone together with hydroxypropyl Me cellulose acetate  
 succinate. The resulting solid dispersion was mixed with hydroxypropyl Me  
 cellulose, lactose, and Mg stearate. The mixt. was finally compressed to  
 give tablets.

IT 67-52-7D, 2,4,6(1H,3H,5H)-Pyrimidinetrione, derivs. 9003-01-4,  
 Polyacrylic acid 9004-38-0, Cellulose acetate phthalate 9004-62-0,  
 Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3,  
 Hydroxypropyl methyl cellulose 9004-67-5, Methyl cellulose 9032-42-2,  
 Hydroxyethyl methyl cellulose 9032-50-2, Methyl cellulose phthalate  
 19216-56-9, Prazosin 21829-25-4, Nifedipine 25086-15-1, Methacrylic  
 acid-methyl methacrylate copolymer 25087-26-7, Polymethacrylic acid  
 25300-64-5, Styrene-maleic acid copolymer 25609-89-6, Crotonic  
 acid-vinyl acetate copolymer 29094-61-9, Glipizide 35795-16-5,  
 Trimazosin 37324-30-4, Hydroxypropyl cellulose phthalate 52907-01-4,

Cellulose acetate trimellitate 53237-50-6 54391-89-8, Cellulose acetate terephthalate 54910-89-3, Fluoxetine 56509-23-0, Sodium cellulose acetate phthalate 67165-96-2, Hydroxypropyl methyl cellulose acetate phthalate 68130-20-1, Starch phthalate 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 74191-85-8, Doxazosin 76974-66-8, Hydroxypropyl cellulose acetate succinate 79617-96-2, Sertraline 88527-84-8, Amylose acetate phthalate 89233-51-2, Cellulose propionate phthalate 93413-69-5, Venlafaxine 96299-43-3, Styrene-maleic acid-dibutyl phthalate copolymer 96352-13-5, Hydroxypropyl ethyl cellulose phthalate 139755-83-2, Sildenafil 146939-27-7, Ziprasidone 167077-74-9 167077-75-0, Cellulose butyrate trimellitate **186392-65-4** 188979-58-0 252856-84-1, Poly(vinyl acetate hydrogen phthalate) 288141-80-0, Methyl cellulose acetate phthalate 288154-33-6 288156-14-9 288297-68-7 288297-69-8 288307-47-1, Hydroxyethyl methyl cellulose acetate phthalate 288307-48-2, Hydroxyethyl methyl cellulose acetate succinate 288307-50-6, Hydroxypropyl cellulose butyrate phthalate 288307-51-7, Cellulose acetate isophthalate

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(cellulosic polymer and pH-sensitive polymer matrixes for solid dispersion of low-soly. drugs)

IT 9001-03-0, Carbonic anhydrase **9035-74-9**, Glycogen phosphorylase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**; cellulosic polymer and pH-sensitive polymer matrixes for solid dispersion of low-soly. drugs)

L36 ANSWER 8 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:566034 HCAPLUS

DOCUMENT NUMBER: 131:199699

TITLE: N-[(Substituted five-membered di- or triaza diunsaturated ring)carbonyl]guanidine derivatives for the treatment of ischemia

INVENTOR(S): Hamanaka, Ernest S.; Guzman-Perez, Angel; Ruggeri, Roger B.; Wester, Ronald T.; Mularski, Christian J.

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 246 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943663	A1	19990902	WO 1999-IB206	19990205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2321642	AA	19990902	CA 1999-2321642	19990205
AU 9920706	A1	19990915	AU 1999-20706	19990205
AU 739403	B2	20011011		
BR 9908332	A	20001107	BR 1999-8332	19990205
EP 1056729	A1	20001206	EP 1999-901083	19990205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				

SI, LT, LV, FI, RO

JP 2002504546	T2	20020212	JP 2000-533420	19990205
ZA 9901578	A	20000828	ZA 1999-1578	19990226
NO 2000004192	A	20000822	NO 2000-4192	20000822

PRIORITY APPLN. INFO.:	US 1998-76362P	P	19980227
	WO 1999-IB206	W	19990205

OTHER SOURCE(S): MARPAT 131:199699

AB Guanidine derivs. ZCON:C(NH2)2 [I; Z = certain (un)substituted, diunsatd., diazoles and triazoles] and their pharmaceutically acceptable salts and/or prodrugs are disclosed, for use as inhibitors of sodium-hydrogen exchanger type 1 (NHE-1). Also disclosed are methods of using I, and pharmaceutical compns. contg. them. I are useful for the redn. of tissue damage resulting from tissue ischemia (no data). A large no. of compds. I and their intermediates were prepd. and/or specifically claimed. For instance, guanidine-HCl was converted to the free base, taken up in THF-DMF mixt., and coupled with 5-methyl-2-(2-methoxyphenyl)-2H-1,2,3-triazole-4-carboxylic acid (pre-activated with carbonyldiimidazole), and the resultant guanidine deriv. was isolated and acidified with HCl in MeOH, to give title compd. II.HCl in 17% yield.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT Brain, disease  
**Heart, disease**  
 Intestine, disease  
 Kidney, disease  
 Liver, disease  
 Lung, disease  
 Muscle, disease  
 Pancreas, disease  
 Spleen

(**ischemia**; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of **ischemia**)

IT **Ischemia**  
 (prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

IT 9028-31-3, Aldose reductase **9035-74-9**, Glycogen phosphorylase  
 RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(pharmaceuticals also contg. **inhibitors** of; prepn. of diazole and triazole guanidine derivs. as NHE-1 **inhibitors** for treatment of ischemia)

IT 110703-94-1, 3,4-Dihydro-4-oxo-3-[[5-(trifluoromethyl)-2-benzothiazolyl]methyl]-1-phthalazineacetic acid 186392-40-5  
 186392-43-8 186392-49-4 186392-53-0 186392-64-3 **186392-65-4**  
 186429-64-1 186429-78-7 186429-91-4 186430-03-5 186430-23-9  
 186430-41-1 186430-57-9 186431-27-6 225929-30-6

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pharmaceuticals contg.; prepn. of diazole and triazole guanidine derivs. as NHE-1 inhibitors for treatment of ischemia)

L36 ANSWER 9 OF 9 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:193899 HCAPLUS

DOCUMENT NUMBER: 130:227741

TITLE: Solid pharmaceutical dispersions with enhanced bioavailability

INVENTOR(S): Curatolo, William John; Herbig, Scott Max; Nightingale, James Alan Schriver

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 46 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 901786	A2	19990317	EP 1998-305960	19980727
EP 901786	A3	20000119		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207896	A	19990217	CN 1998-116282	19980810
JP 11116502	A2	19990427	JP 1998-227328	19980811
JP 2984661	B2	19991129		
BR 9803144	A	20000111	BR 1998-3144	19980811
US 2002009494	A1	20020124	US 2001-770562	20010126

PRIORITY APPLN. INFO.:  
 US 1997-55221P P 19970811  
 US 1998-131019 B1 19980807

AB Spray dried solid dispersions comprising a sparingly sol. drug and hydroxypropyl Me cellulose acetate succinate (HPMCAS) provide increased aq. soly. and/or bioavailability in a use environment. Spray dried compns. were prepd. from HPMCAS and compds. such as ziprasidone, griseofulvin, nifedipine and phenytoin.

IT 9015-71-8, Corticotropin releasing hormone 9035-74-9, Glycogen phosphorylase 80619-02-9, 5-Lipoxygenase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; solid pharmaceutical dispersions with enhanced bioavailability)

IT 57-41-0, Phenytoin 126-07-8, Griseofulvin 21829-25-4, Nifedipine 71138-97-1, Hydroxypropyl methyl cellulose acetate succinate 146939-27-7, Ziprasidone 175139-41-0 175140-00-8 186392-43-8 186392-65-4 221163-46-8  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (solid pharmaceutical dispersions with enhanced bioavailability)

=> FIL STNGUIDE

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FILE CONTAINS CURRENT INFORMATION.  
 LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L37

L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR  
 PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI

L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)

L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT  
 OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR  
 PKT OR DMA)/RL

L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT  
 OR DIABETES MELLITUS+NT,PFT/CT

L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC  
 CARDIOMYOPATHY"+PFT/CT

L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/C  
 T

L7 20270 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOPATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT OR ISCHEMIA+NT,PFT/CT

L8 9348 SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR "REPERFUSION (L) INJURY"+PFT/CT

L9 335374 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8)

L15 1 SEA FILE=REGISTRY ABB=ON PLU=ON 186392-67-6/RN *claim 2, 6th compound*

L22 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L15

L29 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L22

L31 2 SEA FILE=HCAPLUS ABB=ON PLU=ON W0199639384/PN OR W0199639385/PN

L37 1 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 NOT L31

=> FIL REG

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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L15

L15 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 186392-67-6 REGISTRY

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methyl-2-pyridinylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-(methyl-2-pyridinylamino)-3-oxo-1-(phenylmethyl)propyl]-, [R-(R\*,S\*)]-

FS STEREOSEARCH

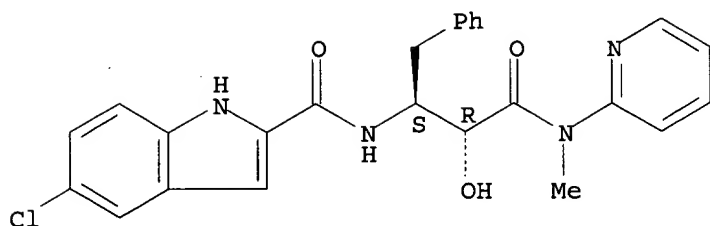
MF C25 H23 Cl N4 O3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

FILE 'HCAPLUS' ENTERED AT 12:09:22 ON 05 SEP 2002

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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10

FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> D IBIB AB HIT L37

L37 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:554794 HCAPLUS

DOCUMENT NUMBER: 135:132447

TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123
PRIORITY APPLN. INFO.:			US 2000-177770P	P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

IT **Blood vessel, disease**  
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**  
(diabetic cardiomyopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Cardiovascular system**  
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

IT **Heart, disease**  
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**  
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT **Heart, disease**  
(ischemia; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)

IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 186392-49-4 186392-65-4 **186392-67-6** 186392-70-1

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and

other cardiovascular diseases)  
IT 9035-74-9, Glycogen phosphorylase  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen  
phosphorylase **inhibitors** for treatment of diabetic  
cardiomyopathy and other cardiovascular diseases)

=> FIL STNGUIDE

FILE 'STNGUIDE' ENTERED AT 12:09:38 ON 05 SEP 2002  
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AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Aug 30, 2002 (20020830/UP).

=> D QUE L38

L1 6031 SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+PFT/CT OR  
PHOSPHORYLASE B+PFT/CT OR 9035-74-9#/OBI  
L2 465 SEA FILE=HCAPLUS ABB=ON PLU=ON L1 (L) (INHIBIT? OR ANTAGONI?)  
L3 153 SEA FILE=HCAPLUS ABB=ON PLU=ON (ANTIDIABETIC AGENTS+NT,PFT/CT  
OR CARDIOVASCULAR AGENTS+NT,PFT/CT) (L) (THU OR BAC OR PAC OR  
PKT OR DMA)/RL  
L4 47128 SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT,PFT/CT  
OR DIABETES MELLITUS+NT,PFT/CT  
L5 304 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC  
CARDIOMYOPATHY"+PFT/CT  
L6 287453 SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT,PFT/C  
T  
L7 20270 SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) CARDIOMYOP  
ATHY, ISCHEMIC"+PFT/CT OR "HEART, DISEASE (L) ISCHEMIA"+PFT/CT  
OR ISCHEMIA+NT,PFT/CT  
L8 9348 SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR  
"REPERFUSION (L) INJURY"+PFT/CT  
L9 335374 SEA FILE=HCAPLUS ABB=ON PLU=ON (L2 OR L3 OR L4 OR L5 OR L6  
OR L7 OR L8)  
L16 1 SEA FILE=REGISTRY ABB=ON PLU=ON 186392-70-1/RN  
L23 4 SEA FILE=HCAPLUS ABB=ON PLU=ON L16  
L30 3 SEA FILE=HCAPLUS ABB=ON PLU=ON L9 AND L23  
L31 2 SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR WO199639385/  
PN  
L38 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L30 NOT L31

*7th compound,  
claim 2*

=> FIL REG

FILE 'REGISTRY' ENTERED AT 12:10:22 ON 05 SEP 2002  
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STRUCTURE FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3  
DICTIONARY FILE UPDATES: 4 SEP 2002 HIGHEST RN 446821-48-3

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> D L16

L16 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS

RN 186392-70-1 REGISTRY

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]-, [R-(R\*,S\*)]-

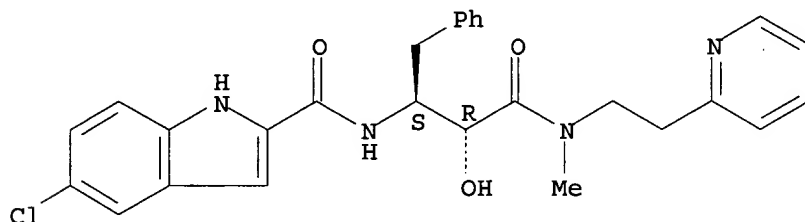
FS STEREOSEARCH

MF C27 H27 Cl N4 O3

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> FIL HCAPLUS

FILE 'HCAPLUS' ENTERED AT 12:10:35 ON 05 SEP 2002

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FILE COVERS 1907 - 5 Sep 2002 VOL 137 ISS 10

Searched by Thom Larson, STIC, 308-7309

FILE LAST UPDATED: 4 Sep 2002 (20020904/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=&gt; D IBIB AB HIT L38 1-2

L38 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:709687 HCAPLUS

DOCUMENT NUMBER: 135:272869

TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 78 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319
PRIORITY APPLN. INFO.:		US 2000-191381P P 20000322		
OTHER SOURCE(S): MARPAT 135:272869				
<p>AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH<sub>2</sub>, CH-alkyl when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6- or 7-NO<sub>2</sub>, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R<sub>2</sub> = H; R<sub>3</sub> = H, alkyl; R<sub>4</sub> = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R<sub>5</sub> = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R<sub>7</sub> = H, F, alkyl; or R<sub>5</sub> and R<sub>7</sub> can be taken together to be oxo; R<sub>6</sub> = carboxy, alkoxy-carbonyl, amido, acyl, alkyl, OH, alkoxy; R<sub>9</sub> = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prep'd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF; HOBt, EDC, room temp.) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.</p>				
<p>IT <b>Diabetes mellitus</b> (non-insulin-dependent; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)</p>				
IT 186392-40-5P	186392-46-1P	186392-47-2P	186392-49-4P	186392-51-8P
186392-52-9P	186392-53-0P	186392-64-3P	186392-65-4P	
<b>186392-70-1P</b>	186429-64-1P	186429-91-4P	186430-03-5P	
186430-23-9P	186430-41-1P	186430-83-1P	186431-27-6P	186431-28-7P
186431-29-8P	225929-30-6P	251446-20-5P	251446-21-6P	251446-22-7P
251446-23-8P	251446-24-9P	251446-25-0P	251446-26-1P	251446-27-2P

251446-28-3P	251446-29-4P	251446-30-7P	251446-31-8P	251446-32-9P
251446-33-0P	251446-34-1P	251446-35-2P	332098-11-0P	332098-12-1P
332098-13-2P	332098-14-3P	332098-15-4P	332098-16-5P	332098-17-6P
332098-18-7P	332098-19-8P	332098-20-1P	332098-21-2P	332098-22-3P
332098-23-4P	332098-24-5P	332098-25-6P	332098-26-7P	332098-27-8P
332098-28-9P	332098-29-0P	332098-30-3P	332098-31-4P	332098-32-5P
332098-33-6P	332098-34-7P	332098-35-8P	332098-36-9P	332098-37-0P
332098-38-1P	332098-39-2P	332098-40-5P	332098-41-6P	332098-42-7P
332098-43-8P	332098-44-9P	332098-45-0P	332098-46-1P	332098-47-2P
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332098-55-2P	332098-57-4P	332098-59-6P	332098-61-0P	332098-63-2P
332098-65-4P	362521-64-0P	362521-65-1P	362521-66-2P	362521-89-9P
362521-91-3P				

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)  
(synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L38 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:554794 HCAPLUS

DOCUMENT NUMBER: 135:132447

TITLE: Chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123

PRIORITY APPLN. INFO.: US 2000-177770P P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoylmethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.

- IT **Blood vessel, disease**  
(diabetic angiopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **Heart, disease**  
(diabetic cardiomyopathy; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Cardiovascular system**  
(disease; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **Heart, disease**  
(failure; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Heart, disease**  
(infarction; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT **Heart, disease**  
(**ischemia**; chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of **diabetic cardiomyopathy** and other cardiovascular diseases)
- IT 56-03-1D, Biguanide, derivs. 504-75-6D, Imidazoline, derivs. 7440-62-2D, Vanadium, salts, biological studies 9004-10-8, Insulin, biological studies 97322-87-7D, TroGlitazone, derivs. 186392-21-2 186392-39-2 186392-40-5 186392-49-4 186392-65-4 186392-67-6 186392-70-1  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)
- IT **9035-74-9, Glycogen phosphorylase**  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

# Generic Structure Search

display query  
for line 31  
(L31)

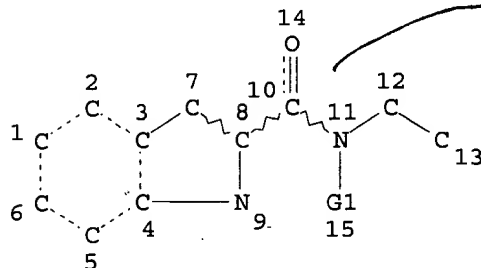
B. Chism; 09/767,633

Page 1

=> d que 131

L1

STR



undefined bonds to allow for  
resonance structures and/or  
tautomer structures.

Ak @16

VAR G1=H/(16) = R3 = H or Alkyl-(see node 16 above).

NODE ATTRIBUTES:

CONNECT IS E2 RC AT 9

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS M1-X5 C AT 16

size of alkyl group @ node 16 is limited  
to minimum of 1 to maximum of 5  
(m1-x5) carbons.

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

L2 (	2665)	SEA FILE=REGISTRY SSS FUL L1	← search of structure in Registry file
L3 (	473)	SEA FILE=HCAPLUS ABB=ON PLU=ON L2	← search Registry hits in HCAPLUS
L4 (	1)	SEA FILE=REGISTRY ABB=ON PLU=ON 9035-74-9/RN	← Registry # for glycogen phosphorylase
L5 (	4127)	SEA FILE=HCAPLUS ABB=ON PLU=ON L4	
L6 (	6031)	SEA FILE=HCAPLUS ABB=ON PLU=ON PHOSPHORYLASE+B+PFT/CT OR L5	
L7 (	465)	SEA FILE=HCAPLUS ABB=ON PLU=ON L6 (L) (INHIBIT? OR ANTAGONI?)	
L8 (	16)	SEA FILE=HCAPLUS ABB=ON PLU=ON L7 AND L3	
L9 (	10520)	SEA FILE=HCAPLUS ABB=ON PLU=ON ANTIDIABETIC AGENTS+NT, PFT/CT	
L10 (	26)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L9	
L11 (	47097)	SEA FILE=HCAPLUS ABB=ON PLU=ON DIABETES INSIPIDUS+NT, PFT/CT OR DIABETES MELLITUS+NT, PFT/CT	
L12 (	14)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L11	
L13 (	304)	SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) DIABETIC CARDIOMYOPATHY"+PFT/CT	
L14 (	3)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L13	
L15 (	57969)	SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR AGENTS+NT, PFT/CT	
L16 (	65)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L15	
L17 (	248)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 (L) (THU OR BAC OR BUU OR DMA)/RL	
L18 (	46)	SEA FILE=HCAPLUS ABB=ON PLU=ON L17 AND L16	
L19 (	287361)	SEA FILE=HCAPLUS ABB=ON PLU=ON CARDIOVASCULAR SYSTEM+NT, PFT/CT	
L20 (	44)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L19	
L21 (	15610)	SEA FILE=HCAPLUS ABB=ON PLU=ON "HEART, DISEASE (L) ISCHEMIA"+PFT/CT	
L22 (	13)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L21	
L23 (	9343)	SEA FILE=HCAPLUS ABB=ON PLU=ON REPERFUSION+PFT/CT OR "REPERFUSION (L) INJURY"+PFT/CT	
L24 (	4)	SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L23	

Point of Contact:  
Thomas G. Larson, Ph.D.  
703-308-7309  
CM1, Rm. 6 B 01

controlled  
vocabulary  
index  
terms  
(1ct)  
that  
correspond  
to key  
words  
listed  
on  
search  
request  
form



combined answer set  
using controlled terms.  
This is the one I  
called you about.  
Page 2

L25 ( 4973)SEA FILE=HCAPLUS ABB=ON PLU=ON ISCHEMIA+NT,PFT/CT  
L26 ( 6)SEA FILE=HCAPLUS ABB=ON PLU=ON L3 AND L25  
L27 ( 93)SEA FILE=HCAPLUS ABB=ON PLU=ON L8 OR L10 OR L12 OR L14 OR  
L18 OR L20 OR L22 OR L24 OR L26  
L28 ( 2)SEA FILE=HCAPLUS ABB=ON PLU=ON WO199639384/PN OR WO199639385/  
PN  
L29 ( 91)SEA FILE=HCAPLUS ABB=ON PLU=ON L27 NOT L28  
L30 ( 334749)SEA FILE=HCAPLUS ABB=ON PLU=ON (((GLYCOGEN/AB (5A) PHOSPHORYL  
?/AB (5A) INHIBIT?/AB) OR (DIABET?/AB) OR (CARDIO?/AB OR  
HEART/AB OR MYOCARDI?/AB) OR (ISCHEMIA/AB (5A) MYOCARD?/AB) OR  
(REPERFUS?/AB OR RE-PERFUS?/AB))) OR (((GLYCOGEN/TI (5A)  
PHOSPHORYL?/TI (5A) INHIBIT?/TI) OR (DIABET?/TI) OR (CARDIO?/TI  
OR HEART/TI OR MYOCARDI?/TI) OR (ISCHEMIA/TI (5A) MYOCARD?/TI)  
OR (REPERFUS?/TI OR RE-PERFUS?/TI)))  
L31 30 SEA FILE=HCAPLUS ABB=ON PLU=ON L29 AND L30

remove  
inventors  
priority  
documents  
Search free  
text of  
abstract  
(Ab) and  
title (Ti)  
with terms  
listed on  
search re-  
quest form.

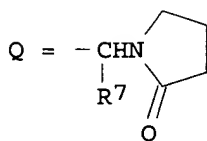
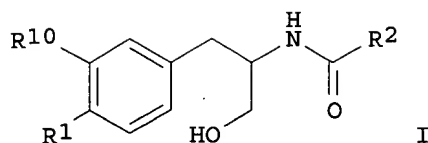
(final answer set)  
=> D IBIB ABS HITSTR 1-30 - print answer set

L31 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2002 ACS  
ACCESSION NUMBER: 2002:484863 HCAPLUS  
DOCUMENT NUMBER: 137:47448  
TITLE: Preparation of substituted phenylalaninol derivatives  
as protein tyrosine phosphatase inhibitors  
INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John E.;  
Liljebris, Charlotta; Schostarez, Heinrich Josef;  
Barf, Tjeerd; Nilsson, Marianne  
PATENT ASSIGNEE(S): USA  
SOURCE: U.S., 144 pp., Cont.-in-part of U.S. Ser. No. 138,642.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6410585	B1	20020625	US 1999-265410	19990310
US 6353023	B1	20020305	US 1998-138642	19980824
WO 2000053583	A1	20000914	WO 2000-US6022	20000309
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1161421	A1	20011212	EP 2000-917793	20000309
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			

PRIORITY APPLN. INFO.: US 1997-57730P P 19970828  
US 1998-138642 A2 19980824  
US 1999-265410 A 19990310  
WO 2000-US6022 W 20000309

OTHER SOURCE(S): MARPAT 137:47448  
GI



AB The invention comprises phenylalaninol derivs., e.g., I [R1 = OSO3H, OCH(CO2R5)2, OCH2CO2R5, OCH(CO2R5)CH2CO2R5, OC(CO2R5):CHCO2R5, CH2CH(CO2R5)2, CH:C(CO2R5)2, OCH2CONHOH, N(CH2CO2R5)2, OCHFCO2R5 (R5 = H, alkyl, alkylphenyl); R2 = CHR7NHXR6, group Q (R6 = alkyl, alkyl-CONH2, alkyl-NHCO2R5, etc.; R7 = H, any group given for R6); R10 = H, CO2R5, CONHOH, 5-tetrazolyl, F, OCH2CO2R5], or their pharmaceutically acceptable salts, as small mol. wt., non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent **diabetes** mellitus. Thus, 5-[(2S)-2-[[[(2S)-2-[(tert-butoxycarbonyl)amino]-3-phenylpropanoyl]amino]-3-hydroxypropyl]-2-(carboxymethoxy)benzoic acid (claimed compd.) was prepd. and showed 80% inhibition of protein tyrosine phosphatase 1B at a concn. of 10 .mu.M.

IT 292833-72-8P 292833-82-0P 292833-93-3P

292834-05-0P 292834-16-3P 292834-26-5P

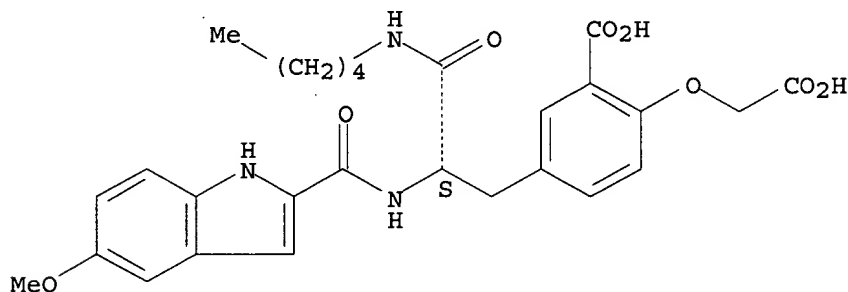
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)

(prepn. of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 292833-72-8 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxo-3-(pentylamino)propyl]- (9CI) (CA INDEX NAME)

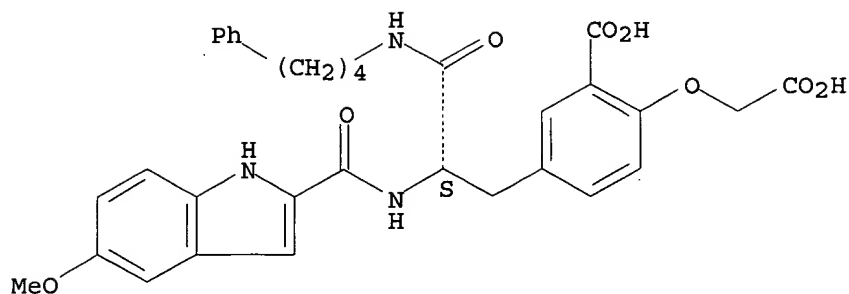
Absolute stereochemistry.



RN 292833-82-0 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-3-oxo-3-[(4-phenylbutyl)amino]propyl]- (9CI) (CA INDEX NAME)

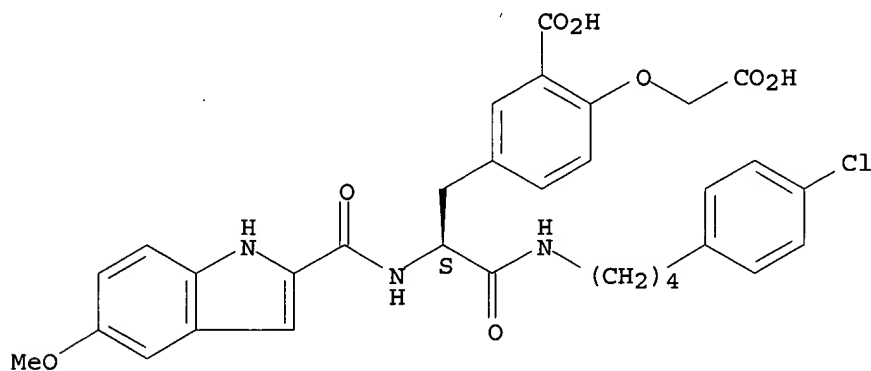
Absolute stereochemistry.



RN 292833-93-3 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-3-[[4-(4-chlorophenyl)butyl]amino]-2-[[5-methoxy-1H-indol-2-yl]carbonyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

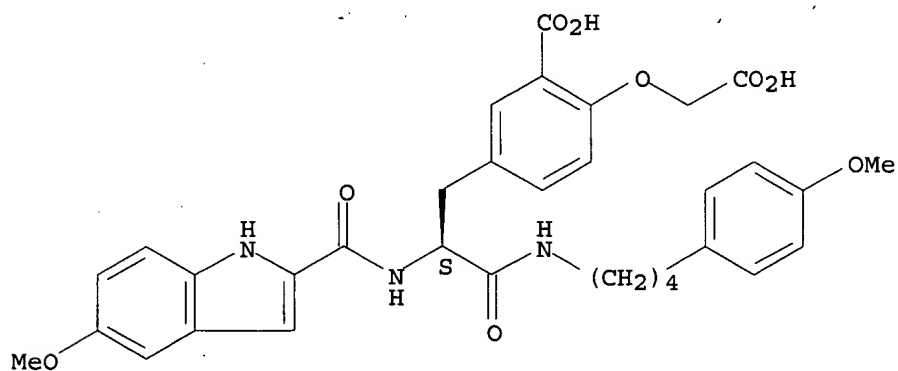
Absolute stereochemistry.



RN 292834-05-0 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[5-methoxy-1H-indol-2-yl]carbonyl]amino]-3-[[4-(4-methoxyphenyl)butyl]amino]-3-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

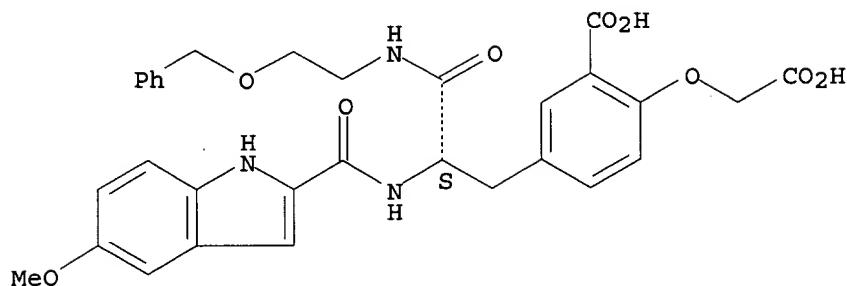


RN 292834-16-3 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[5-methoxy-1H-indol-2-yl]carbonyl]amino]-3-oxo-3-[[2-(phenylmethoxy)ethyl]amino]propyl]- (9CI)

(CA INDEX NAME)

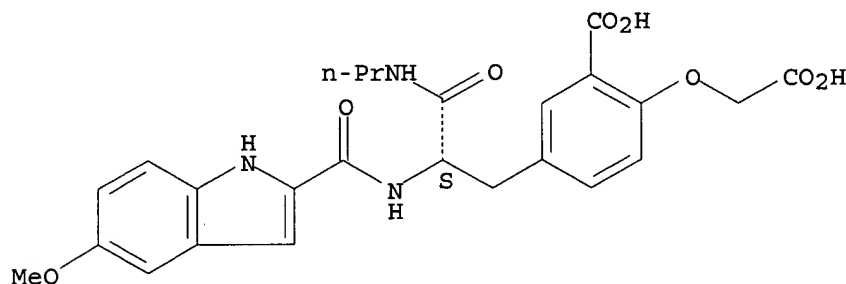
Absolute stereochemistry.



RN 292834-26-5 HCAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-2-[[[5-methoxy-1H-indol-2-yl]carbonyl]amino]-3-oxo-3-(propylamino)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:309882 HCAPLUS

DOCUMENT NUMBER: 136:325415

TITLE: Preparation of mono- and bis-indolylquinones as GRB-2 adaptor protein inhibitors for treatment of cell proliferative disorders and insulin-related disorders

INVENTOR(S): Tang, Peng Cho; McMahon, Gerald; Harris, G. Davis, Jr.; Lipson, Ken

PATENT ASSIGNEE(S): USA

SOURCE: U.S., 41 pp., Cont.-in-part of U.S. Ser. No. 6,090,838.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6376529	B1	20020423	US 1999-405244	19990924
US 5780496	A	19980714	US 1996-658337	19960605
US 5786488	A	19980728	US 1997-964791	19971105
US 6110957	A	20000829	US 1998-72861	19980505

US 6090838 A 20000718 US 1998-90737 19980604  
 WO 2001021589 A2 20010329 WO 2000-US26235 20000925  
 WO 2001021589 A3 20020117

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
 CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,  
 HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,  
 LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,  
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,  
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,  
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1218342 A2 20020703 EP 2000-965395 20000925

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.:

US 1995-476136 B2 19950607  
 US 1996-658337 A1 19960605  
 US 1996-30604P P 19961113  
 US 1997-42989P P 19970414  
 US 1997-964791 A3 19971105  
 US 1998-72861 A2 19980505  
 US 1998-90737 A2 19980604  
 US 1999-405244 A1 19990924  
 WO 2000-US26235 W 20000925

OTHER SOURCE(S): MARPAT 136:325415

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\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [wherein A = mono- or bicyclic aryl, heteroaryl, (alkyl)carboxy, alkyl(aryl), alkynyl, alkenylcarboxy, hydroxy(alkyl), alkoxy, NO<sub>2</sub>, halo, trihalomethyl, amido, carboxamido, sulfonyl, sulfonamido, amino, mercapto, or 2-methylbut-2-en-4-yl; R<sub>1</sub> and R<sub>2</sub> = independently H, halo, OH, or OCOR; R = alkyl(aryl) or aryl; R<sub>1a</sub> and R<sub>2a</sub> = independently H, alkyl, alkenyl, alkynyl, or (alkyl)aryl; R<sub>3</sub>-R<sub>6</sub> and R<sub>8</sub>-R<sub>11</sub> = independently H, alkyl(carboxy), alkenyl(carboxy), alkynyl, (alkyl)aryl, hydroxy(alkyl), alkoxy, NO<sub>2</sub>, halo, trihalomethyl, amido, carboxamido, carboxy, sulfonyl, sulfonamido, amino, mercapto, or 2-methylbut-2-en-4-yl; R<sub>12</sub> = H, mono- or bicyclic aryl, heteroaryl, alkyl(carboxy), alkenyl(carboxy), alkynyl, (alkyl)aryl, hydroxy(alkyl), alkoxy, NO<sub>2</sub>, halo, trihalomethyl, amido, carboxamido, carboxy, sulfonyl, sulfonamido, amino, mercapto, or 2-methylbut-2-en-4-yl; with provisos; or pharmaceutically acceptable salts thereof] were prepd. as GRB-2 adaptor protein inhibitors. I are useful for ameliorating the symptoms of cell proliferative disorders assocd. with CRB-2 adaptor protein function and for treating insulin-related disorders, such as **diabetes**, insulin resistance, insulin deficiency, and insulin allergy. For example, a mixt. of tetrabromo-1,4-benzoquinone, 2-phenylindole, and Cs<sub>2</sub>CO<sub>3</sub> in AcCN was stirred at room temp. for 3 h. Addn. of 2-(3-methylbutyl)indole, stirring at room temp. for 24 h, and heating to 85.degree.C with THF, EtOH, and KOH for 10 h afforded II. The latter effectively bound tyrosine phosphorylated EGF-receptor to a GRB-2 SH2 peptide domain, inhibited A431 vulvar carcinoma tumor cell growth in vivo by 49% at 75 mg/kg/day and 55% at 100 mg/kg/day, gave an EC<sub>50</sub> of 6.5 .mu.M in the LDH cytotoxicity assay, and both stimulated phosphorylation of insulin receptor tyrosine kinase and allowed deactivation of the insulin receptor in NIH 3T3 cells.

IT 331632-13-4P, 3-[2-(N-Butylcarboxamido)indol-3-yl]-6-(2-butyldiol-

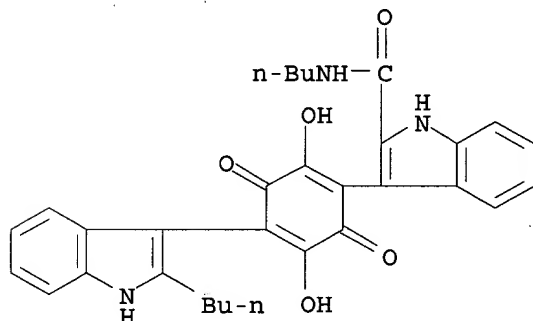
3-yl)-2,5-dihydroxy-1,4-quinone

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(GRB-2 inhibitor; prepn. of indolylquinones as GRB-2 adaptor protein inhibitors for treatment of cell proliferative disorders and insulin-related disorders)

RN 331632-13-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-butyl-3-[4-(2-butyl-1H-indol-3-yl)-2,5-dihydroxy-3,6-dioxo-1,4-cyclohexadien-1-yl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 119 THERE ARE 119 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:170712 HCAPLUS

DOCUMENT NUMBER: 136:365703

TITLE: The 1.76 .ANG. resolution crystal structure of glycogen phosphorylase b complexed with glucose, and CP 320626, a potential antidiabetic drug

AUTHOR(S): Oikonomakos, Nikos G.; Zographos, Spyros E.; Skamnaki, Vicky T.; Archontis, Georgios

CORPORATE SOURCE: Institute of Biological Research and Biotechnology, The National Hellenic Research Foundation, Athens, 11635, Greece

SOURCE: Bioorganic & Medicinal Chemistry (2002), 10(5), 1313-1319

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

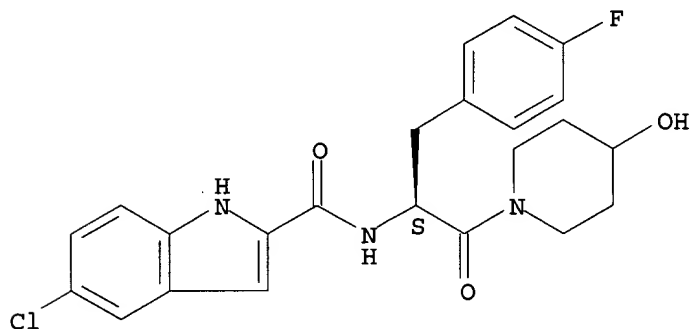
DOCUMENT TYPE: Journal

LANGUAGE: English

AB CP 320626, a potential antidiabetic drug, **inhibits glycogen phosphorylase (I)** in synergism with glucose. To elucidate the structural basis of synergistic inhibition, the authors detd. the crystal structure of muscle I complexed with both glucose and CP 320626 at 1.76 .ANG. resolu., and refined it to a crystallog. R value of 0.211 (Rfree = 0.235). CP 320626 was found to bind at a novel allosteric site, which was .apprx.33 .ANG. from the catalytic site, where glucose binds. The high-resoln. structure allowed unambiguous definition of the conformation of the 1-acetyl-4-hydroxy-piperidine ring supported by theor. energy calcns. Both CP 320626 and glucose promoted the less active T-state, thereby explaining their synergistic inhibition. Structural comparison of the I.cntdot.glucose.cntdot.CP 320626 complex with liver glycogen phosphorylase a (II) complexed with a related compd. (CP 403700)

showed that the ligand binding site was conserved in II.  
 IT 186430-23-9D, CP 320626, complexes with phosphorylase b and glucose  
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (crystal structure of phosphorylase b complexed with glucose and CP 320626, a potential antidiabetic drug)  
 RN 186430-23-9 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2002:104618 HCAPLUS  
 DOCUMENT NUMBER: 136:145214  
 TITLE: Use of **glycogen phosphorylase inhibitors** to inhibit tumor growth  
 INVENTOR(S): Krasner, Alan Seth  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: Eur. Pat. Appl., 28 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1177791	A2	20020206	EP 2001-306440	20010727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002128673	A2	20020509	JP 2001-226129	20010726
US 2002123513	A1	20020905	US 2001-919205	20010731
PRIORITY APPLN. INFO.:			US 2000-221717P	P 20000731
OTHER SOURCE(S): MARPAT 136:145214				
AB The invention relates to the use of <b>glycogen phosphorylase inhibitors</b> to inhibit abnormal cell growth in mammals, including humans. The invention also relates to pharmaceutical compns. contg. <b>glycogen phosphorylase inhibitors</b> alone or in combination with other <b>glycogen phosphorylase inhibitors</b> or other <b>inhibitors</b> of abnormal cell growth, and to methods of treating cancer,				

hyperproliferative disorders, or abnormal cell growth in a mammal by administering to a mammal in need thereof the compds. and compns. of the invention.

IT **9012-69-5P**, Glycogen phosphorylase B  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)  
 (glycogen phosphorylase **inhibitor** to **inhibit** tumor growth)  
 RN 9012-69-5 HCAPLUS  
 CN Phosphorylase b (9CI) (CA INDEX NAME)

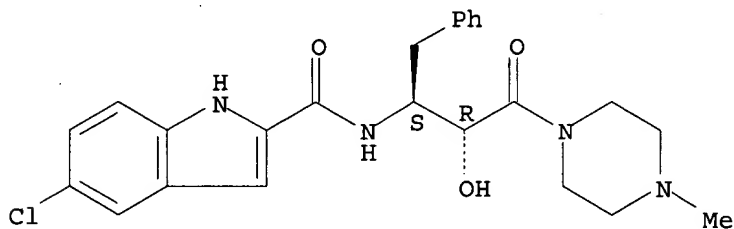
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT **9035-74-9P**, Glycogen phosphorylase  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
 (glycogen phosphorylase **inhibitor** to **inhibit** tumor growth)  
 RN 9035-74-9 HCAPLUS  
 CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT **186392-09-6 186392-46-1 186392-47-2 186392-51-8 186392-52-9 186392-53-0 186392-64-3 186429-66-3 186430-04-6 186430-23-9 186430-40-0 186431-27-6 186431-28-7 208830-24-4 208830-25-5**  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (glycogen phosphorylase inhibitor to inhibit tumor growth)  
 RN 186392-09-6 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-methyl-1-piperazinyl)-3-oxo-1-(phenylmethyl)propyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

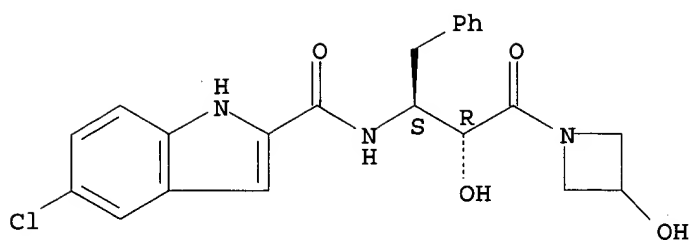


● HCl

RN 186392-46-1 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(3-hydroxy-1-azetidiny)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

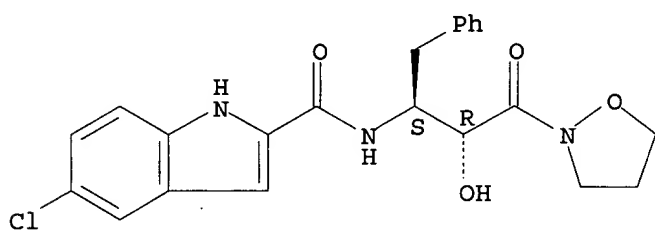




RN 186392-47-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(2-isoxazolidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

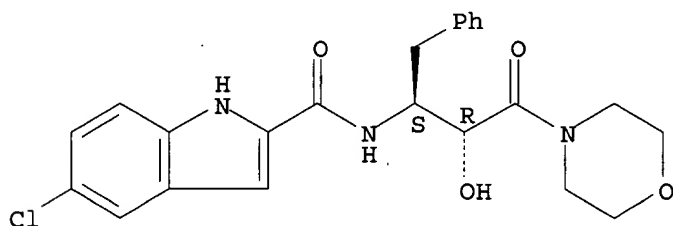
Absolute stereochemistry.



RN 186392-51-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-morpholinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

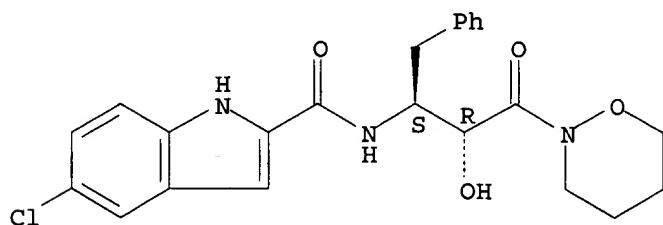
Absolute stereochemistry.



RN 186392-52-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-oxo-1-(phenylmethyl)-3-(tetrahydro-2H-1,2-oxazin-2-yl)propyl]- (9CI) (CA INDEX NAME)

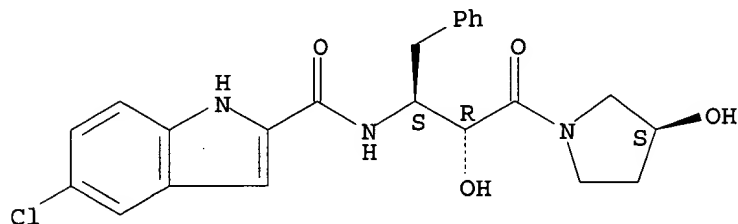
Absolute stereochemistry.



RN 186392-53-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

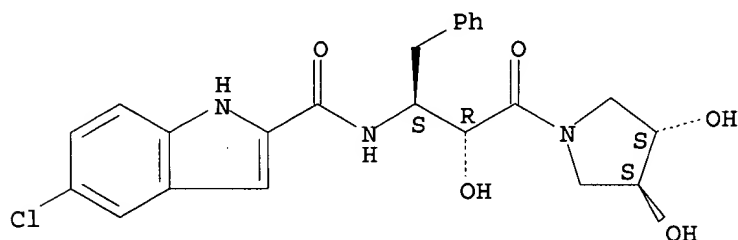
Absolute stereochemistry.



RN 186392-64-3 HCAPLUS

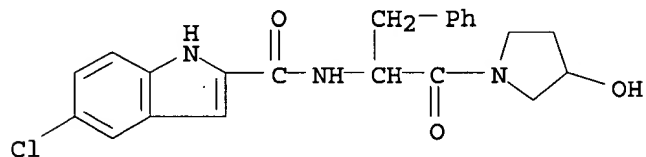
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



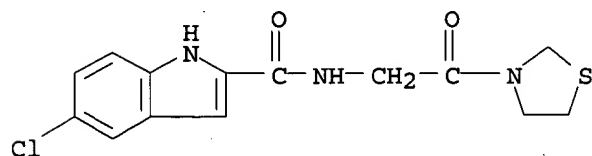
RN 186429-66-3 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(3-hydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)



RN 186430-04-6 HCAPLUS

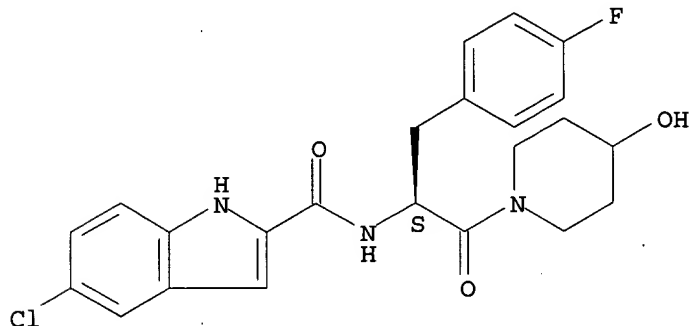
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-oxo-2-(3-thiazolidinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

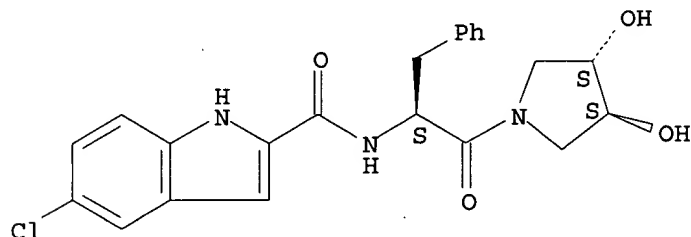
Absolute stereochemistry.



RN 186430-40-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

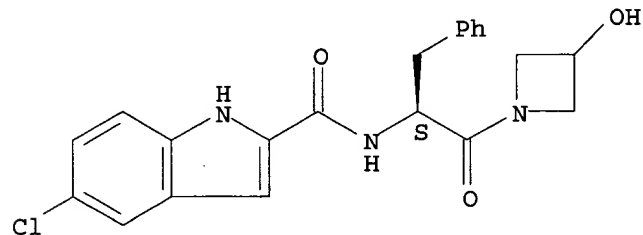
Absolute stereochemistry.



RN 186431-27-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

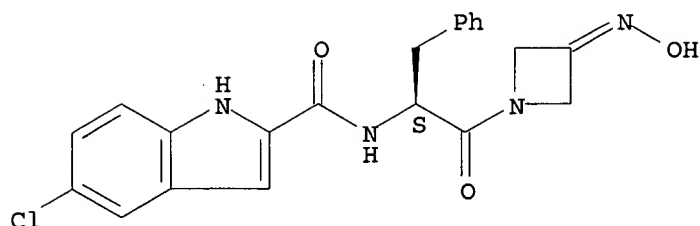
Absolute stereochemistry.



RN 186431-28-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-azetidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

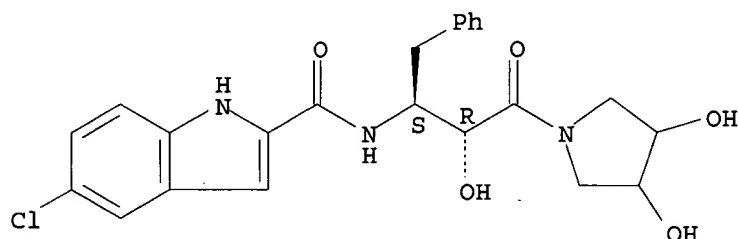
Absolute stereochemistry.



RN 208830-24-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

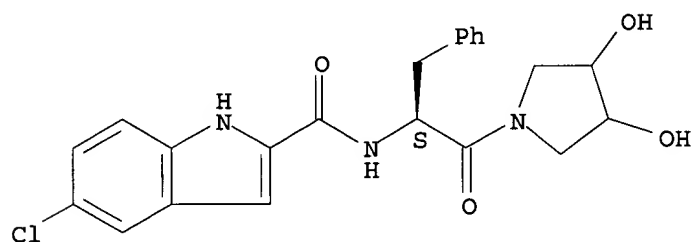
Absolute stereochemistry.



RN 208830-25-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3,4-dihydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:10432 HCAPLUS

DOCUMENT NUMBER: 136:85669

TITLE: Preparation of (e.g.) N-alkylaryl-N-aryl-N'-aryl ureas as glucagon antagonists/inverse agonists

INVENTOR(S): Jorgensen, Anker Steen; Christensen, Inge Thoger; Kodra, Janos Tibor; Madsen, Peter; Behrens, Carsten; Sams, Christian; Lau, Jesper

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.

SOURCE: PCT Int. Appl., 201 pp.

CODEN: PIXXD2

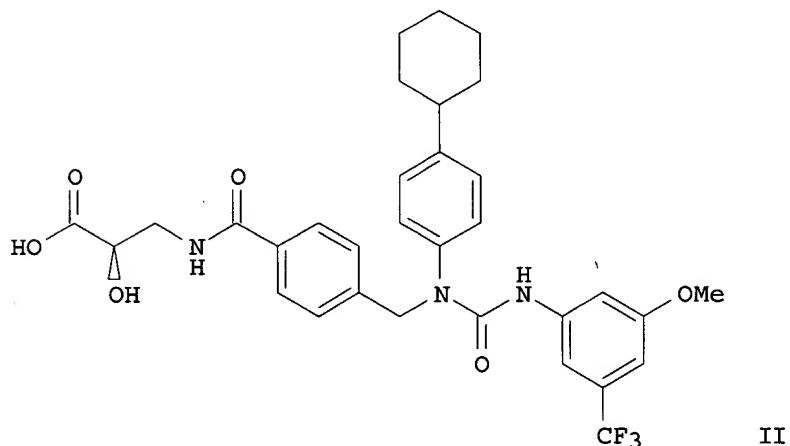
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000612	A1	20020103	WO 2001-DK435	20010621
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 2001065834 A5 20020108 AU 2001-65834 20010621 PRIORITY APPLN. INFO.: DK 2000-984 A 20000623 DK 2000-1734 A 20001117 WO 2001-DK435 W 20010621				
OTHER SOURCE(S): MARPAT 136:85669				
GI				



AB Title compds. R1OC(O)-A-CR2R3-N(R4)-C(O)-Z-CHR5-N(E)-X-D [R1-5 = H, alkyl; A = C(O), CH-alkoxy, CHF; Z = (un)substituted arylene or a divalent radical derived from a 5 or 6 membered heteroarom. ring contg. 1 or 2 heteroatoms selected from N, O and S; X = alkyl, acyl, amido, etc.; D = (un)substituted Ph, naphthyl, pyridyl, benzothiophenyl, etc.; E = (un)substituted cyclohexyl, Ph, benzyl, phenethyl, etc.; I] were prepd. Examples include data for 73 compds., two glucagon receptor binding assays and a glucose-dependent insulinotropic peptide (GIP) receptor binding assay. E.g., 4-cyclohexylaniline was reductively alkylated with 4-formyl benzoic acid Me ester (MeOH, HOAc, NaCNBH<sub>3</sub>) in 87% yield. The amine was added to an isocyanate derived from 5-methoxy-3-trifluoromethylaniline (prepn. given; CH<sub>2</sub>Cl<sub>2</sub>, room temp.) to give a urea as an oil that was sapond. (EtOH, NaOH, room temp., 16 h) to give the solid carboxylic acid in 49% yield. The carboxylic acid was coupled to (R)-isoserine Et ester (DMF, HOBt, EDAC) followed by hydrolysis to give example compd. II as a cryst. solid. In a glucagon receptor binding assay, compds. of the

invention had IC50 < 1500 nM and many were below 250 nM. I are useful in the treatment or prevention of any diseases wherein a glucagon antagonistic action is beneficial, such as hyperglycemia, type 1 **diabetes**, type 2 **diabetes**, disorders of lipid metab. and obesity.

IT **385836-75-9P**

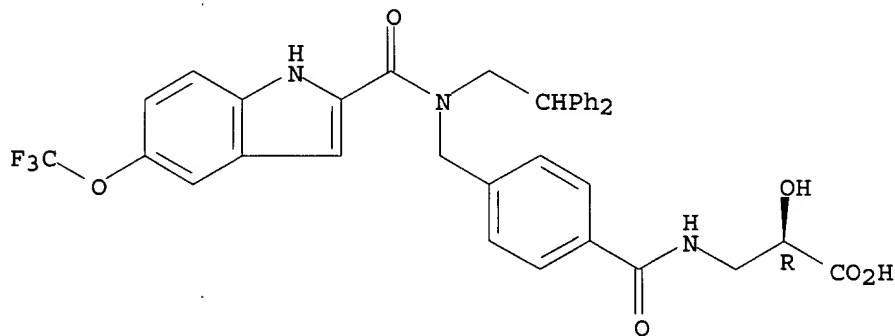
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); **THU** (**Therapeutic use**); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; prepn. of N-alkylaryl-N'-aryl-N'-aryl ureas as glucagon antagonists/inverse agonists)

RN 385836-75-9 HCAPLUS

CN Propanoic acid, 3-[[4-[[[(2,2-diphenylethyl)[[5-(trifluoromethoxy)-1H-indol-2-yl]carbonyl]amino]methyl]benzoyl]amino]-2-hydroxy-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:936092 HCAPLUS

DOCUMENT NUMBER: 136:53752

TITLE: Synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors

INVENTOR(S): Mylari, Banavara L.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 41 pp.

CODEN: USXXCO

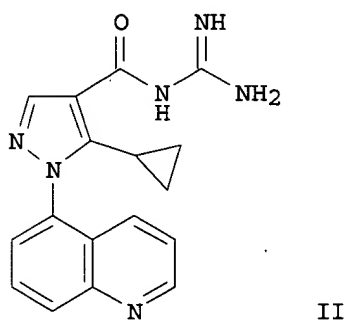
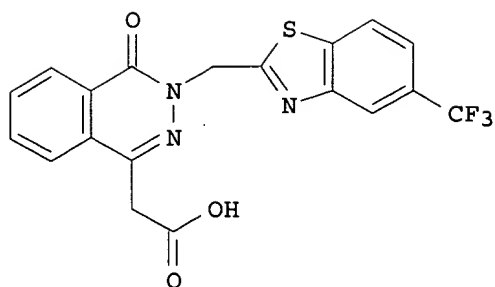
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001056095	A1	20011227	US 2001-782798	20010213
PRIORITY APPLN. INFO.: GI			US 2000-183004P P	20000216



AB Mono-, di- and triethanolamine salts of [4-Oxo-(5-trifluoromethylbenzothiazol-2-ylmethyl)-3,4-dihydrophthalazin-1-yl]acetic acid (zopolrestat; I) were prepd. E.g., a soln. of I in acetone was added to ethanolamine (10 mol equiv, room temp., 1 h) which afforded, after purifn., the ethanolamine salt in 95% yield, m.p. 119 - 121.degree.C. Ethanolamine salts of I are used alone or with NHE-1 inhibitors (e.g. II), selective serotonin reuptake **inhibitors** (SSRIs, e.g. fluoxetine), **glycogen phosphorylase inhibitors** (GPIs), sorbitol dehydrogenase **inhibitors** (SDIs) and antihypertensive agents for treating **diabetic** complications.

IT **186392-65-4**

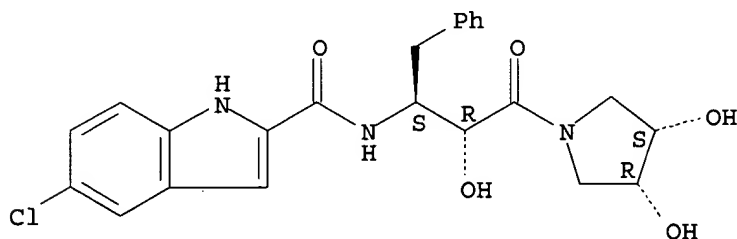
RL: PAC (Pharmacological activity); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)

(combination pharmaceutical; synthesis and use of mono-, di- and triethanolamine salts of zopolrestat alone and in combination with (e.g.) NHE-1 inhibitors)

RN 186392-65-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9035-74-9, Glycogen phosphorylase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(synthesis and use of mono-, di- and triethanolamine salts of  
zopolrestat alone and in combination with (e.g.) NHE-1  
inhibitors)

RN 9035-74-9 HCAPLUS

CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L31 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:709687 HCAPLUS

DOCUMENT NUMBER: 135:272869

TITLE: Synthesis of indolyl-amides as **glycogen  
phosphorylase inhibitors** for  
treatment of type 2 **diabetes**

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 78 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

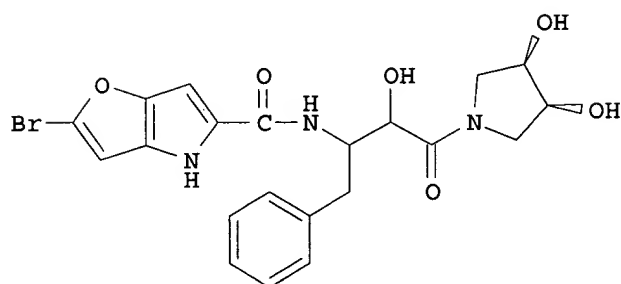
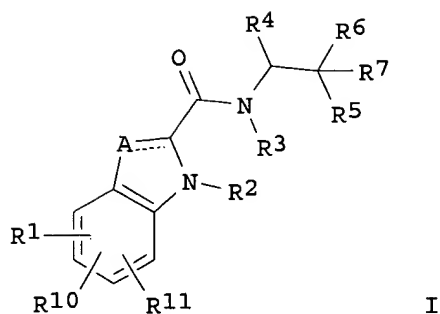
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136071	A2	20010926	EP 2001-301979	20010305
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2001302546	A2	20011031	JP 2001-78839	20010319
PRIORITY APPLN. INFO.:			US 2000-191381P	P 20000322
OTHER SOURCE(S):		MARPAT 135:272869		
GI				





AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH<sub>2</sub>, CH-alkyl when the dotted line is not a bond; R<sub>1</sub>, R<sub>10</sub>, R<sub>11</sub> = H, halo, 4-, 6- or 7-NO<sub>2</sub>, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R<sub>2</sub> = H; R<sub>3</sub> = H, alkyl; R<sub>4</sub> = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R<sub>5</sub> = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R<sub>7</sub> = H, F, alkyl; or R<sub>5</sub> and R<sub>7</sub> can be taken together to be oxo; R<sub>6</sub> = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R<sub>9</sub> = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepd. Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBT, EDC, room temp.) to give amide II. Compds. I are **glycogen phosphorylase inhibitors** used for treating type 2 **diabetes** mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-**glycogen phosphorylase** inhibiting anti-diabetic agents are also claimed.

IT 186392-40-5P 186392-46-1P 186392-47-2P  
 186392-49-4P 186392-51-8P 186392-52-9P  
 186392-53-0P 186392-64-3P 186392-65-4P  
 186392-70-1P 186429-64-1P 186429-91-4P  
 186430-03-5P 186430-23-9P 186430-41-1P  
 186430-83-1P 186431-27-6P 186431-28-7P  
 186431-29-8P 225929-30-6P 362521-64-0P  
 362521-65-1P 362521-66-2P 362521-89-9P  
 362521-91-3P

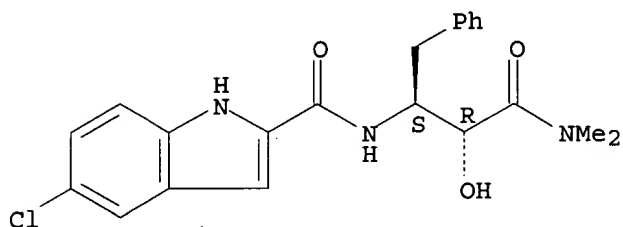
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

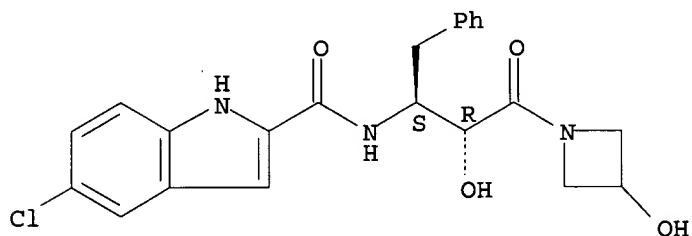
Absolute stereochemistry.



RN 186392-46-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(3-hydroxy-1-azetidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

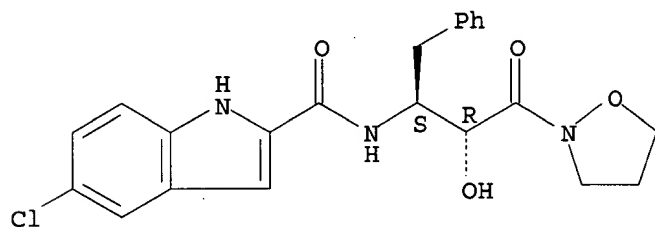
Absolute stereochemistry.



RN 186392-47-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(2-isoxazolidinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

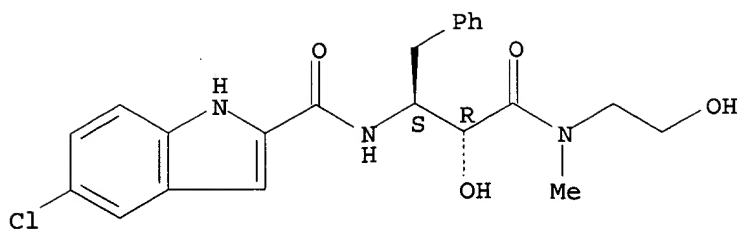
Absolute stereochemistry.



RN 186392-49-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

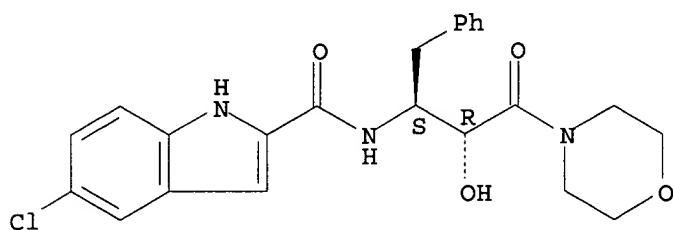
Absolute stereochemistry.



RN 186392-51-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-morpholinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

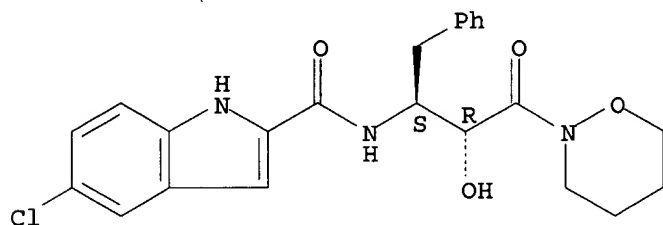
Absolute stereochemistry.



RN 186392-52-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-oxo-1-(phenylmethyl)-3-(tetrahydro-2H-1,2-oxazin-2-yl)propyl]- (9CI) (CA INDEX NAME)

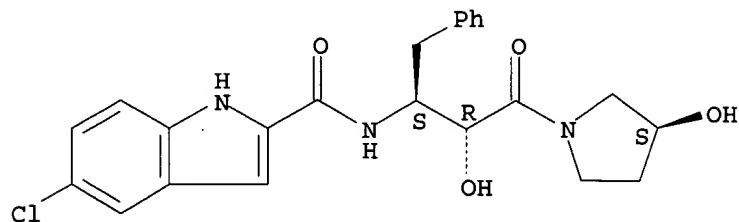
Absolute stereochemistry.



RN 186392-53-0 HCAPLUS

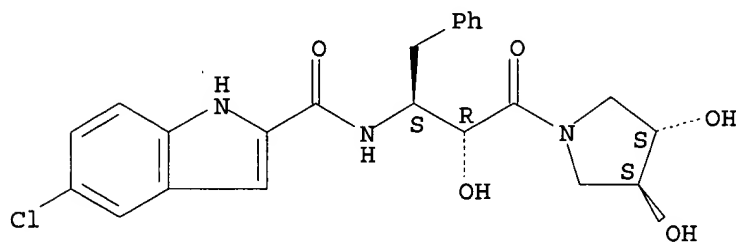
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



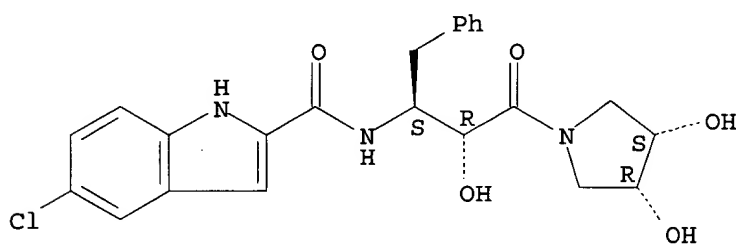
RN 186392-64-3 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



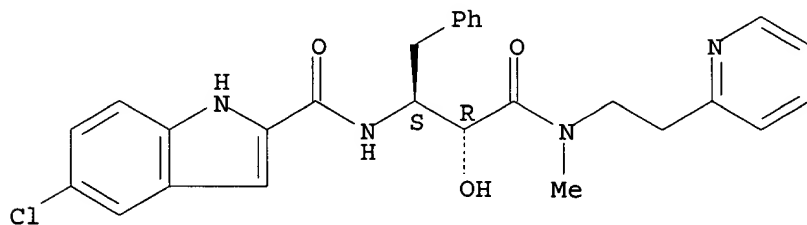
RN 186392-65-4 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



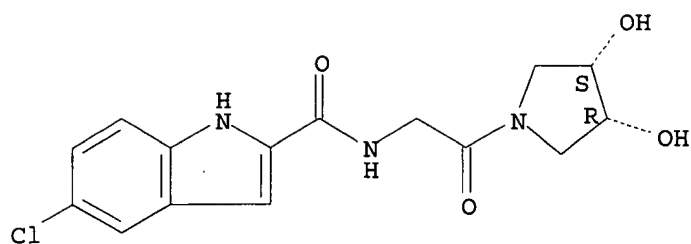
RN 186392-70-1 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186429-64-1 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]-, rel- (9CI) (CA INDEX NAME)

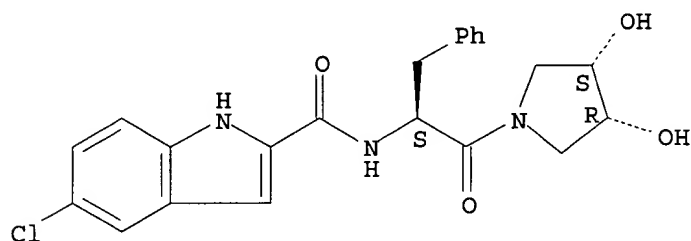
Relative stereochemistry.



RN 186429-91-4 HCAPLUS

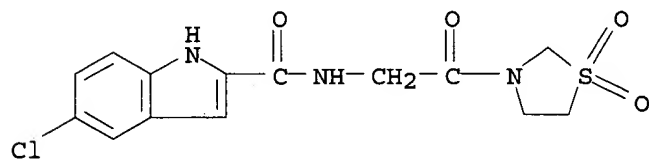
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186430-03-5 HCAPLUS

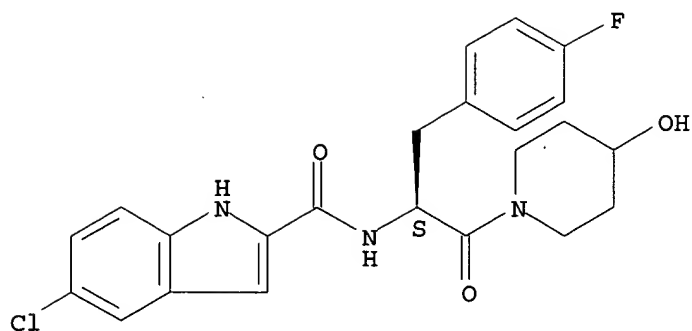
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(1,1-dioxido-3-thiazolidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

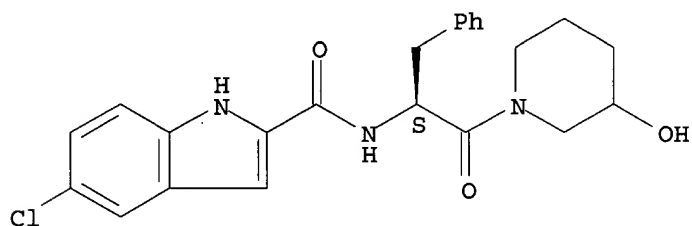
Absolute stereochemistry.



RN 186430-41-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-piperidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

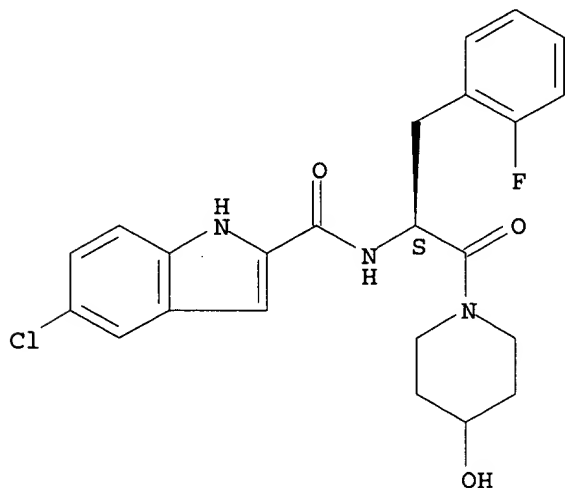
Absolute stereochemistry.



RN 186430-83-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(2-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

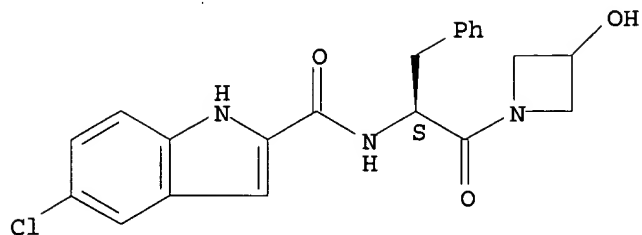
Absolute stereochemistry.



RN 186431-27-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

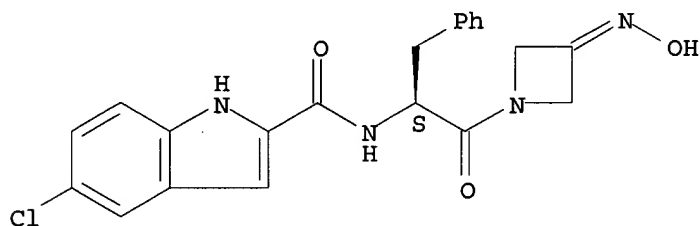
Absolute stereochemistry.



RN 186431-28-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-azetidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

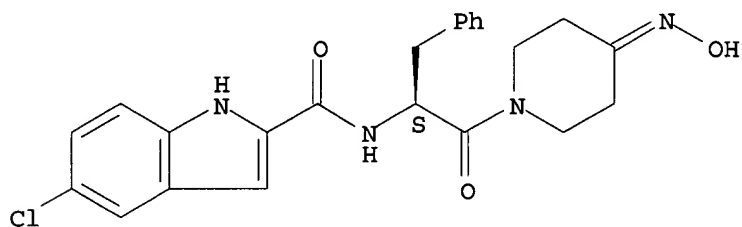
Absolute stereochemistry.



RN 186431-29-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[4-(hydroxyimino)-1-piperidiny]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

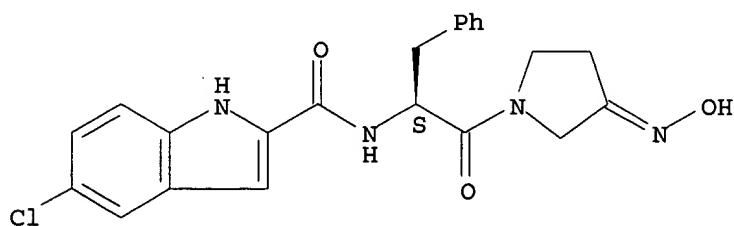


RN 225929-30-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

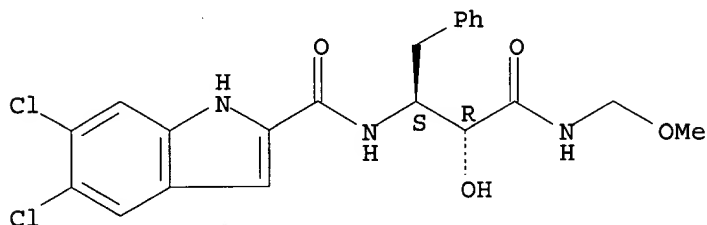
Absolute stereochemistry.

Double bond geometry unknown.



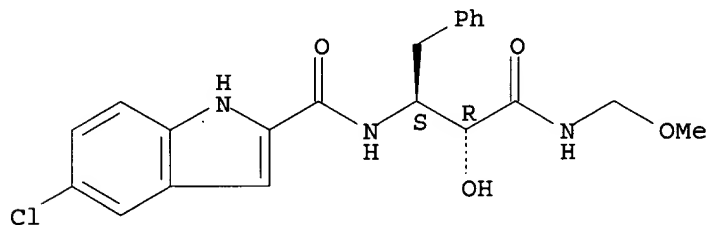
RN 362521-64-0 HCAPLUS  
CN 1H-Indole-2-carboxamide, 5,6-dichloro-N-[(1S,2R)-2-hydroxy-3-  
[(methoxymethyl) amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



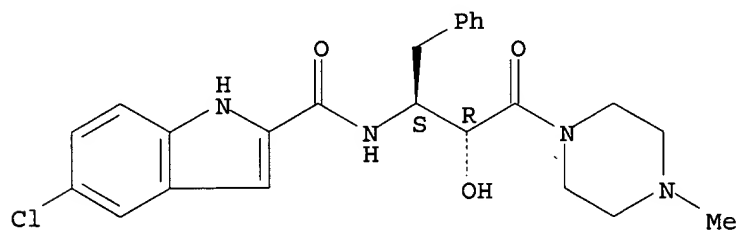
RN 362521-65-1 HCAPLUS  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-  
[(methoxymethyl) amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



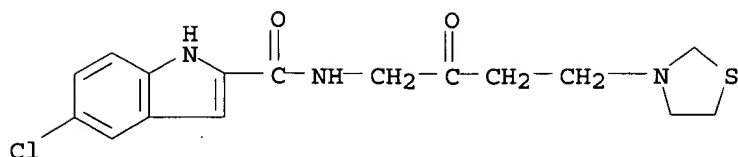
RN 362521-66-2 HCAPLUS  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-methyl-1-  
piperazinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

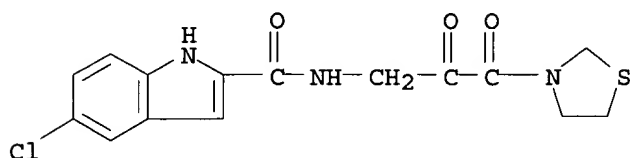


RN 362521-89-9 HCAPLUS  
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-oxo-4-(3-thiazolidinyl)butyl]-  
(9CI) (CA INDEX NAME)





RN 362521-91-3 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2,3-dioxo-3-(3-thiazolidinyl)propyl]-  
(9CI) (CA INDEX NAME)

IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL  
(Biological study)(synthesis of indolyl-amides as glycogen phosphorylase  
inhibitors for treatment of type 2 diabetes)

RN 9035-74-9 HCAPLUS

CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L31 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:693088 HCAPLUS

DOCUMENT NUMBER: 135:262225

TITLE: Glycogen phosphorylase  
inhibitor compositionsINVENTOR(S): Babcock, Walter C.; Friesen, Dwayne Thomas; Lorenz,  
Douglas Alan; Macri, Christopher A.; Nightingale,  
James Alan Schriver; Shanker, Ravi Mysore; Hancock,  
Bruno Caspar; Crew, Marshall D.

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 116 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068092	A2	20010920	WO 2001-IB389	20010316
WO 2001068092	A3	20020321		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,  
CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,  
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,  
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,  
RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,  
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 2001053791 A1 20011220 US 2001-808559 20010314

PRIORITY APPLN. INFO.: US 2000-190125P P 20000316

AB Pharmaceutical compns. of a particularly effective sparingly sol.

**glycogen phosphorylase inhibitor** are disclosed. Thus, an amorphous solid dispersion contg. 25% a drug and 75% polymer was made by first mixing the drug in acetone together with a finely powd. HPMCAS to form a soln. The soln. comprised 1.25% drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray via a 2-fluid external mix spray nozzle at 2.6 bar at a 175 to 180 g/min feed rate into a stainless steel chamber of a NIRO XP spray drier, maintained at a temp. of 180.degree. at the inlet and 69.degree. at the outlet.

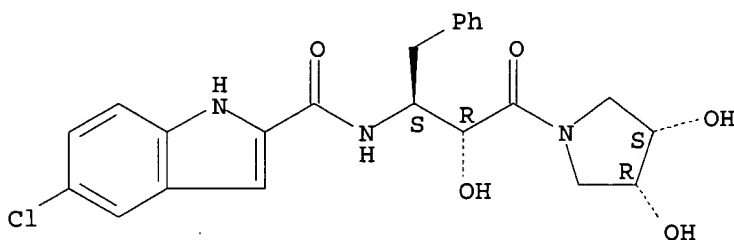
IT 186392-65-4

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (glycogen phosphorylase inhibitor compns.)

RN 186392-65-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9035-74-9, Glycogen phosphorylase

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitor; glycogen phosphorylase inhibitor compns.)

RN 9035-74-9 HCAPLUS

CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L31 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:693054 HCAPLUS

DOCUMENT NUMBER: 135:247221

TITLE: Pharmaceutical compositions containing  
**glycogen phosphorylase inhibitors**

INVENTOR(S): Hoover, Dennis Jay; Shanker, Ravi Mysore; Friesen, Dwayne Thomas; Lorenz, Douglas Alan; Nightingale, James Alan Schriver

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

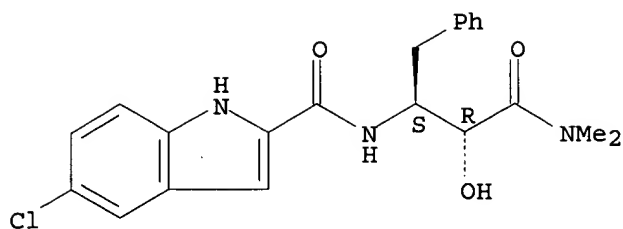
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001068055	A1	20010920	WO 2001-IB394	20010316
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2001053778	A1	20011220	US 2001-805828	20010314
PRIORITY APPLN. INFO.:			US 2000-189942P P 20000316	
OTHER SOURCE(S): MARPAT 135:247221				
AB	Pharmaceutical compns. comprise a <b>glycogen phosphorylase inhibitor</b> and at least one concn.-enhancing polymer. The compn. may be a simple phys. mixt. of <b>glycogen phosphorylase inhibitor</b> and concn.-enhancing polymer or a dispersion of <b>glycogen phosphorylase inhibitor</b> and polymer. A dispersion of 25% 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-3-oxypropyl]amide and 75% polymer was made by first mixing the drug in acetone together with HPMCAS to form a soln. The soln. comprised 1.25 drug, 3.75% HPMCAS, and 95% acetone. This soln. was then spray-dried by directing an atomizing spray using a 2-fluid external-mix spray nozzle at 2.6 bar at a feed rate of 175 to 180 g/min into the stainless-steel chamber of a spray-dryer, maintained at 180.degree. on the inlet and 69.degree. at the outlet. The resulting amorphous solid spray-dried dispersion was collected and then dried in a solvent tray-dryer by spreading the spray-dried particles onto polyethylene-lined trays to a depth of not >1 cm and then drying them at 40.degree. for at least 8 h.			
IT	9035-74-9, Glycogen phosphorylase RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (inhibitors; pharmaceutical compns. contg. glycogen phosphorylase inhibitors)			
RN	9035-74-9 HCAPLUS			
CN	Phosphorylase (9CI) (CA INDEX NAME)			
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***				
IT	186392-40-5 186392-43-8 186392-51-8 186392-53-0 186392-63-2 186392-65-4 186429-91-4 186430-03-5 186430-23-9 186430-40-0 186430-57-9 186431-27-6 361176-31-0 RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (pharmaceutical compns. contg. glycogen phosphorylase inhibitors)			
RN	186392-40-5 HCAPLUS			
CN	1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)			

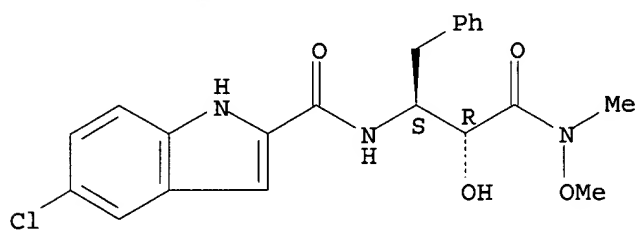
Absolute stereochemistry.



RN 186392-43-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

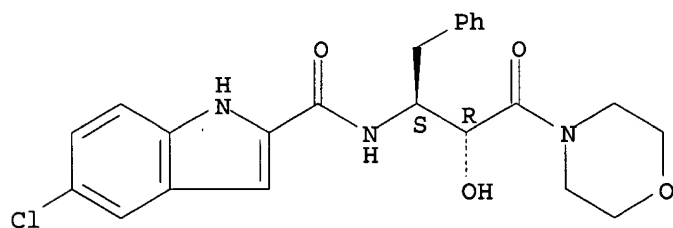
Absolute stereochemistry.



RN 186392-51-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(4-morpholinyl)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

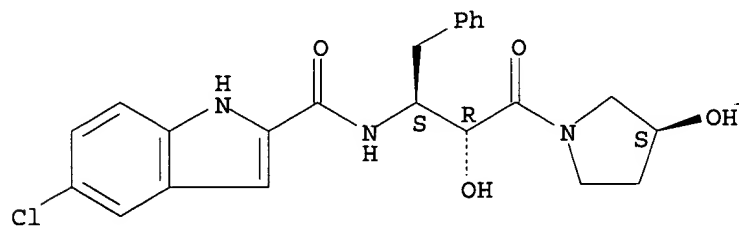
Absolute stereochemistry.



RN 186392-53-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

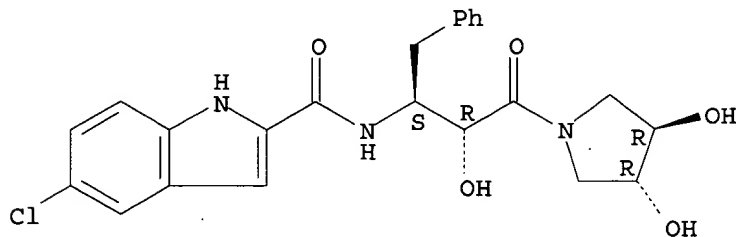
Absolute stereochemistry.



RN 186392-63-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

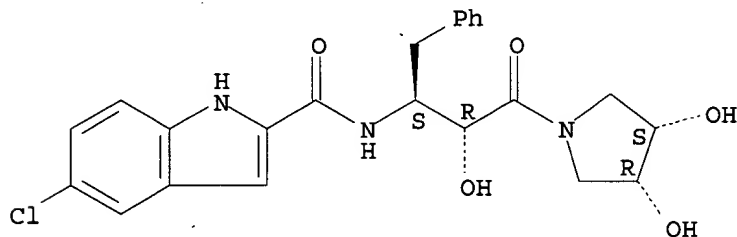
Absolute stereochemistry.



RN 186392-65-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

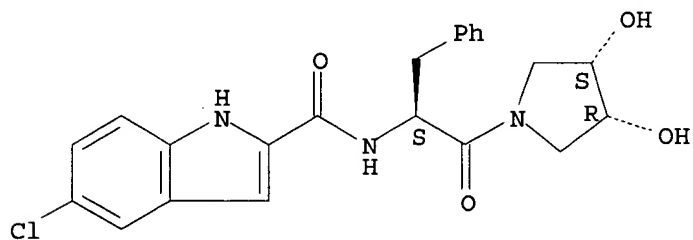
Absolute stereochemistry.



RN 186429-91-4 HCAPLUS

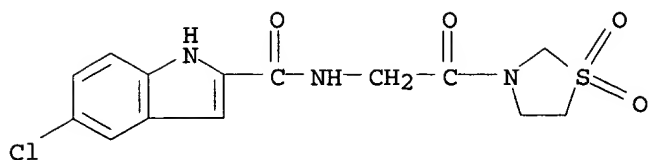
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186430-03-5 HCAPLUS

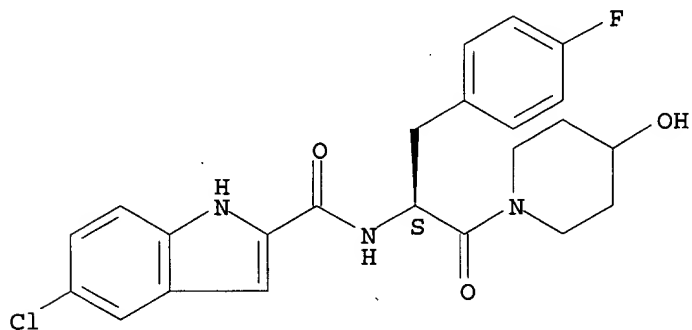
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(1,1-dioxido-3-thiazolidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

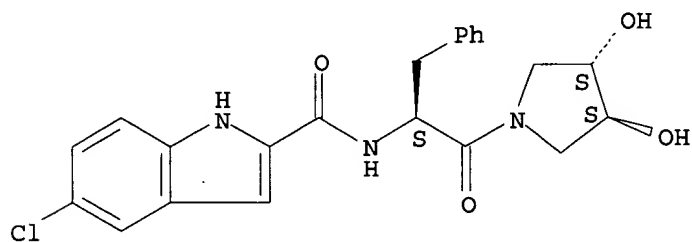
Absolute stereochemistry.



RN 186430-40-0 HCAPLUS

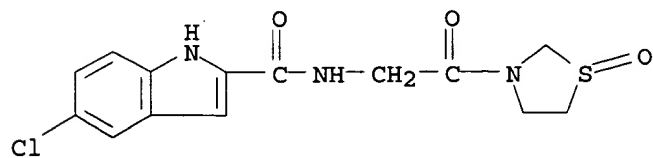
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4S)-3,4-dihydroxy-1-phenylmethyl]pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186430-57-9 HCAPLUS

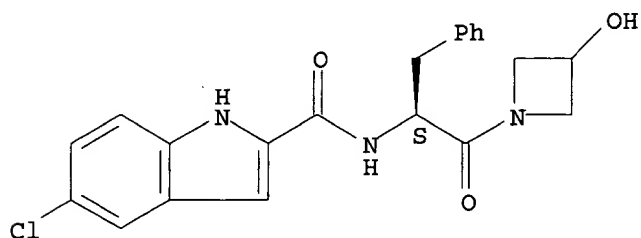
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(1-oxido-3-thiazolidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)



RN 186431-27-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidiny)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

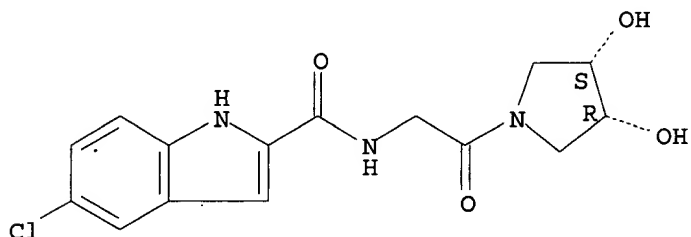
Absolute stereochemistry.



RN 361176-31-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3S,4R)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 10 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:554794 HCAPLUS

DOCUMENT NUMBER: 135:132447

TITLE: Chloroindolephenylethylamide analogs and their prodrugs as **glycogen phosphorylase inhibitors** for treatment of **diabetic cardiomyopathy**

INVENTOR(S): Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Jpn. Kokai Tokkyo Koho, 35 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001206856	A2	20010731	JP 2001-14036	20010123
EP 1125580	A2	20010822	EP 2001-300575	20010123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2001046958	A1	20011129	US 2001-767633	20010123
PRIORITY APPLN. INFO.:			US 2000-177770P	P 20000124

AB Chloroindolephenylethylamide analogs, including 5-chloro-1H-indole-2-

carboxylic acid [(1S)-((R)-hydroxydimethylcarbamoymethyl)-2-phenylethyl]amide, etc., and their prodrugs are claimed as **glycogen phosphorylase inhibitors** for treatment of **diabetic cardiomyopathy**. The title compds. can also combine with insulin, insulin analogs (biguanides), .alpha.2-antagonists, imidazolines, glitazone derivs., PPAR.gamma. agonists, fatty acid oxidn. inhibitors, .alpha.-glucosidase inhibitors, .beta.-agonists, phosphodiesterase inhibitors, hypolipidemics, antiobesity agents, vanadium salts, glucagon antagonists, somatostatin analogs, aldose reductase inhibitors, sorbitol dehydrogenase inhibitors, glucocorticoid receptor antagonists, and/or thyroid hormone analogs for treatment of **diabetes, cardiovascular diseases, heart ischemia, congestive heart failure, hypertension, diabetic angiopathy, myocardial infarction, etc.**

IT 186392-21-2 186392-39-2 186392-40-5  
186392-49-4 186392-65-4 186392-67-6  
186392-70-1

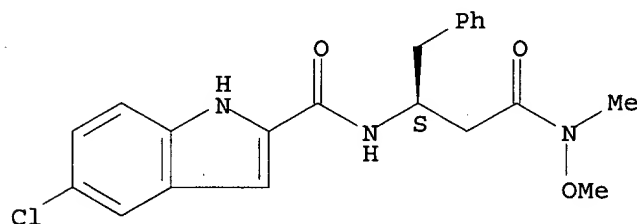
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase inhibitors for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

RN 186392-21-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

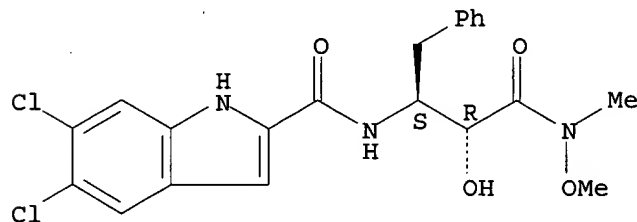
Absolute stereochemistry.



RN 186392-39-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5,6-dichloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

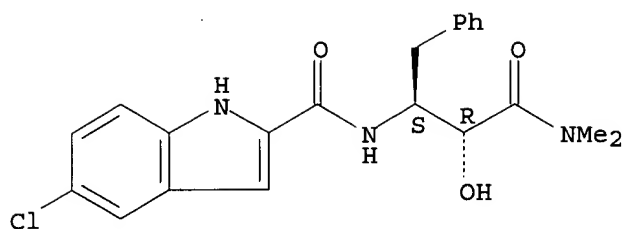


RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

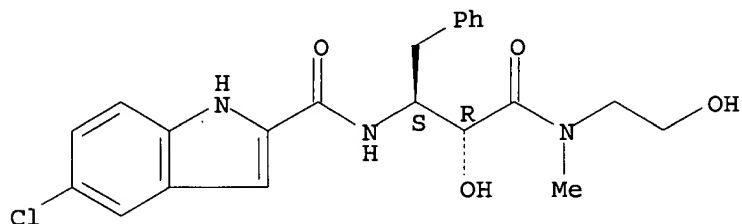




RN 186392-49-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

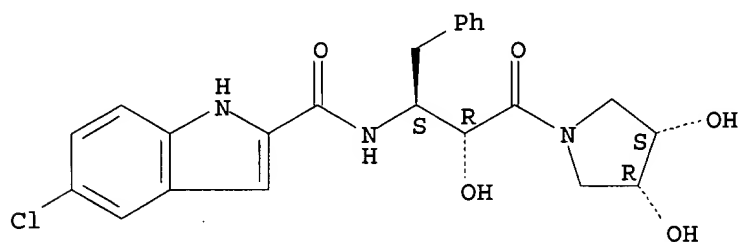
Absolute stereochemistry.



RN 186392-65-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

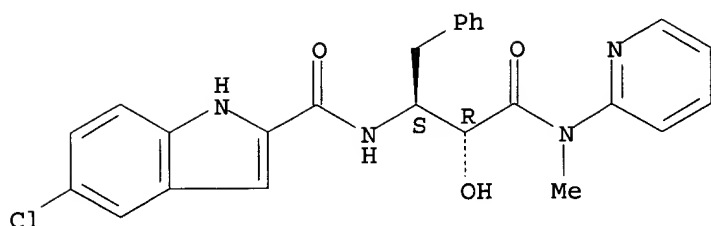
Absolute stereochemistry.



RN 186392-67-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methyl-2-pyridinylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

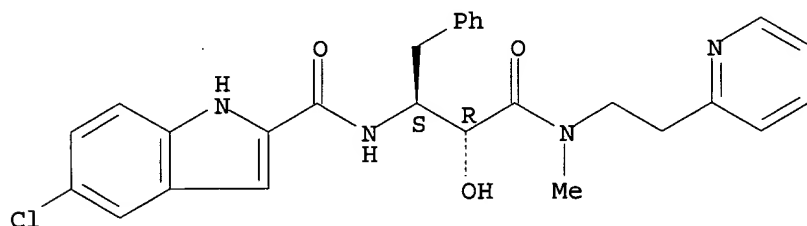
Absolute stereochemistry.



RN 186392-70-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[methyl[2-(2-pyridinyl)ethyl]amino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9035-74-9, Glycogen phosphorylase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(chloroindolephenylethylamide analogs and their prodrugs as glycogen phosphorylase **inhibitors** for treatment of diabetic cardiomyopathy and other cardiovascular diseases)

RN 9035-74-9 HCAPLUS

CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L31 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:435041 HCAPLUS

DOCUMENT NUMBER: 135:33431

TITLE: Preparation of cycloamine as CCR5 receptor antagonists

INVENTOR(S): Shiota, Tatsuki; Yokoyama, Tomonori; Kamimura, Takashi

PATENT ASSIGNEE(S): Teijin Limited, Japan

SOURCE: PCT Int. Appl., 271 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

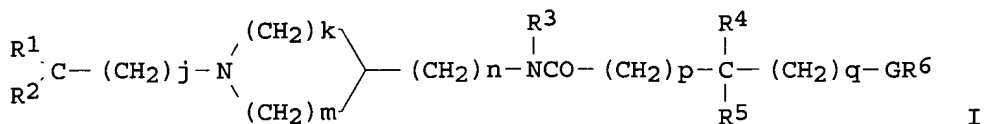
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042208	A1	20010614	WO 2000-JP8627	20001206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,				

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 1999-348778 A 19991208

OTHER SOURCE(S): MARPAT 135:33431

GI



AB Therapeutic or preventive agents for .beta.-chemokine receptor CCR5-related diseases such as AIDS, rheumatoid arthritis, and nephritis, contg. as the active ingredient, cyclic amine derivs. such as piperidine and pyrrolidine derivs. of general formula [I; R1 = (un)substituted Ph, C3-8 cycloalkyl, or arom. heterocyclyl contg. 1-3 heteroatoms of O, S, and/N wherein Ph and arom. heterocyclyl group is optionally condensed to benzene ring or heterocyclyl ring contg. 1-3 heteroatoms of O, S, and/N to form an (un)substituted condensed ring; R2 = H, (un)substituted C1-6 alkyl or Ph, C2-7 alkoxy-carbonyl, HO; j, k = 0-2; m = 2-4; n = 0,1; R3 = H, (un)substituted phenyl-optionally substituted C1-6 alkyl; R4, R5 = H, HO, Ph, (un)substituted C1-6 alkyl; or R4 and R5 together represent a 3-6-membered ring cyclic hydrocarbonyl; p, q = 0,1; G = CO, SO2, CO2, NR7CO, CONR7, NHCONH, NHC(S)NH, NR7SO2, SO2 NR7, NHC(O)2, O2CNH (wherein R7 = H, C1-6 alkyl; or R7 and R5 together form C2-5 alkylene); R6 = (un)substituted C3-8 cycloalkyl, C3-6 cycloalkenyl, Ph, benzyl, or arom. heterocyclyl contg. 1-3 heteroatoms of O, S, and/N, wherein Ph, benzyl, and arom. heterocyclyl are optionally condensed with benzene ring or arom. heterocyclyl group contg. 1-3 heteroatoms of O, S, and/N to form an (un)substituted condensed ring], pharmaceutically acceptable adducts of the same with acids, or pharmaceutically acceptable adducts thereof with C1-6 alkyl, are described. Above CCR5-related diseases include diseases accompanied by destruction of cartilage or bone (in particular chronic rheumatoid arthritis), nephritis or kidney diseases (in particular glomerulonephritis, interstitial nephritis, or nephrosis), demyelinating diseases (in particular multiple sclerosis), post-transplant rejection, host-vs.-graft diseases (GVHD), **diabetes**, chronic obstructive pulmonary diseases (COPD), bronchial asthma, atopic dermatitis, sarcoidosis, fibrosis, arteriosclerosis, psoriasis, and inflammatory bowel diseases. Thus, 3-(trifluoromethylthio)benzoic acid was condensed with (R)-1-(4-chlorobenzyl)-3-(glycylamino)pyrrolidine using diisopropylcarbodiimide and HOBt in tert-butanol and CHCl3 at room temp. for 15 h to give (R)-1-(4-chlorobenzyl)-3-[[N-(3-(trifluoromethylthio)benzoyl)glycyl]aminol]pyrrolidine (II). II and (R)-1-(6-methyl-3-indolylmethyl)-3-[[N-(2-amino-5-(trifluoromethoxy)benzoyl)glycyl]aminol]pyrrolidine 10 .mu.M in vitro inhibited by 20-50% and >80%, resp., the binding of [125I]macrophage inflammatory protein-1.alpha. (MIP-1.alpha.) to CCR5-receptor expressed in CHO cells.

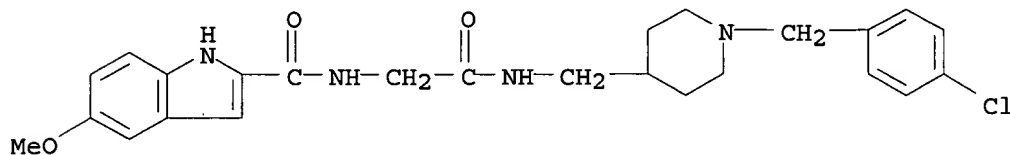
IT 226238-52-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of cycloamine as CCR5 receptor antagonists for therapeutics or remedies of .beta.-chemokine receptor CCR5-related diseases such as AIDS, rheumatoid arthritis, and nephritis)

RN 226238-52-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[[[1-[(4-chlorophenyl)methyl]-4-piperidinyl]methyl]amino]-2-oxoethyl]-5-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:228870 HCAPLUS

DOCUMENT NUMBER: 134:262851

TITLE: Isoxazoline derivative caspase inhibitors for pharmaceutical uses

INVENTOR(S): Kim, Eunice Eun-Kyeong; Park, Mi-Jeong; Lee, Tae-Hee; Chang, Hye-Kyung; Park, Tae-Kyo; Kang, Chang-Yuil; Kim, Young-Myeong; Moon, Kwang-Yul; Oh, Young-Leem; Min, Chang-Hee; Chung, Hyun Ho

PATENT ASSIGNEE(S): LG Chemical Ltd., S. Korea

SOURCE: PCT Int. Appl., 168 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

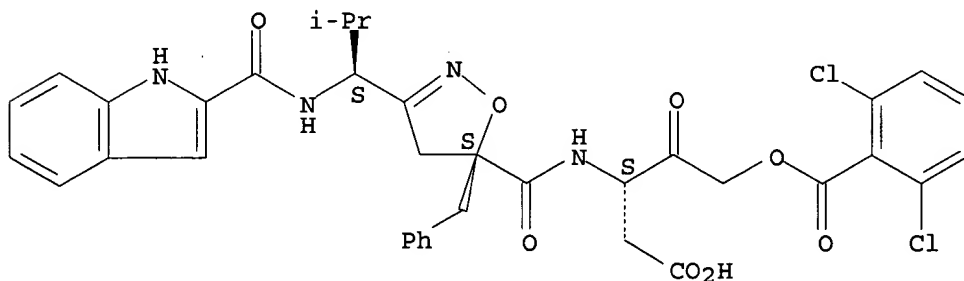
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021600	A1	20010329	WO 2000-KR1047	20000918
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
WO 2001021599	A1	20010329	WO 1999-KR561	19990917
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1212309	A1	20020612	EP 2000-961242	20000918
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,			

R4N(R6)C(=N1O1)CC(R2)C(=O)N(R5)X

IT	332020-92-5P 332020-94-7P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (isoxazoline deriv. caspase inhibitors for pharmaceutical uses)
RN	332020-92-5 HCAPLUS
CN	Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-3-[[[(5S)-4,5-dihydro-3-[(1S)-1-[(1H-indol-2-ylcarbonyl)amino]-2-methylpropyl]-5-(phenylmethyl)-5-isoxazolyl]carbonyl]amino]-2-oxobutyl ester (9CI) (CA INDEX NAME)

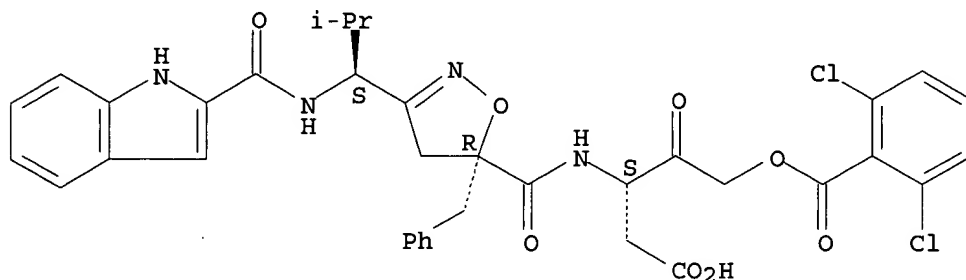
Absolute stereochemistry.



RN 332020-94-7 HCAPLUS

CN Benzoic acid, 2,6-dichloro-, (3S)-4-carboxy-3-[[[(5R)-4,5-dihydro-3-[(1S)-1-[(1H-indol-2-ylcarbonyl)amino]-2-methylpropyl]-5-(phenylmethyl)-5-isoxazolyl]carbonyl]amino]-2-oxobutyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:227614 HCAPLUS

DOCUMENT NUMBER: 135:55802

TITLE: Pharmacology of caspase inhibitors in rabbit **cardiomyocytes** subjected to metabolic inhibition and recovery

AUTHOR(S): Li, Hai Ling; Karwatowska-Prokopczuk, Ewa; Mutomba, Martha; Wu, Joe; Karanewsky, Don; Valentino, Karen; Engler, Robert L.; Gottlieb, Roberta A.

CORPORATE SOURCE: Department of Veterans Affairs Medical Center, Research Service and Department of Medicine, San Diego, CA, 92161, USA

SOURCE: Antioxidants & Redox Signaling (2001), 3(1), 113-123  
CODEN: ARSIF2; ISSN: 1523-0864

PUBLISHER: Mary Ann Liebert

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Protection of ischemic **myocardium** is an important unmet need in **reperfusion** therapy of acute **myocardial** infarction. **Myocardial** ischemia and **reperfusion** induce necrosis and apoptosis in **cardiomyocytes**. Caspase processing and activation are crit. steps in most receptor and nonreceptor pathways of apoptosis. Caspase inhibitors have been shown to reduce ischemia **reperfusion** injury in cardiac muscle. Information about dose response and time of administration are needed to optimize the design of preclin. studies. The authors used isolated adult rabbit **cardiomyocytes** subjected to metabolic inhibition (MI) and recovery to examine the role of caspases and caspase inhibitors, the dose response, and the timing of administration. In vitro inhibitory concns. (Ki) were detd. for purified caspases. **Cardiomyocytes** subjected to MI were treated with peptidomimetic fluoromethyl ketone inhibitors of caspases before or during MI, or at recovery. Caspase inhibitors were most effective when added before MI and included throughout recovery, but were partially protective if added after MI. The optimal concn. of the inhibitors tested was .apprx.10 .mu.M. Protection was sustained when cells were allowed to recover for 4 or 24 h. These results suggest that caspase activation is an important component of myocyte injury mediated by

MI and recovery. Low doses of caspase inhibitors were identified that reduce injury in this model system, and further investigations using in vivo models are warranted.

IT 231950-93-9, IDN 1529

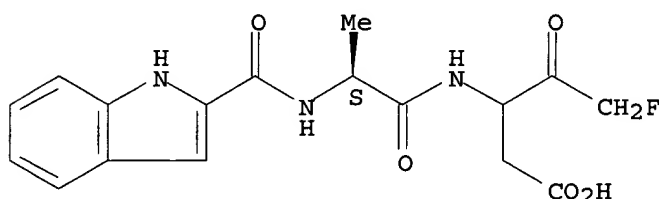
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmacol. of caspase inhibitors in rabbit cardiomyocytes subjected to metabolic inhibition and recovery in relation to treatment of heart ischemia reperfusion injury)

RN 231950-93-9 HCAPLUS

CN Pentanoic acid, 5-fluoro-3-[[[(2S)-2-[(1H-indol-2-ylcarbonyl)amino]-1-oxopropyl]amino]-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:152665 HCAPLUS

DOCUMENT NUMBER: 134:207826

TITLE: Preparation of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and benzopyrans as factor Xa and factor IIa inhibitors

INVENTOR(S): Burns, Christopher J.; Dankulich, William P.; McGarry, Daniel G.; Volz, Francis A.

PATENT ASSIGNEE(S): Aventis Pharmaceuticals Products Inc., USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014358	A2	20010301	WO 2000-IB1562	20000812
WO 2001014358	A3	20010517		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1222182	A2	20020717	EP 2000-968181	20000812
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			

PRIORITY APPLN. INFO.:

US 1999-150767P P 19990826

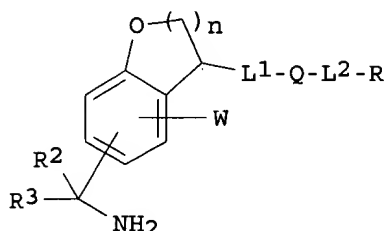
GB 1999-24155 A 19991012

WO 2000-IB1562 W 20000812

OTHER SOURCE(S):

MARPAT 134:207826

GI



AB The title compds. [I;  $n = 1$  or  $2$ ;  $W$  is H or a ring system substituent;  $R$  is hydrogen, cyano, cycloalkyl, cycloalkenyl, heterocyclyl, fused arylcycloalkyl, fused heteroaryl cycloalkyl, etc.;  $R_1$  is hydrogen, alkyl, aralkyl, heteroaralkyl, acyl, aroyl, heteroaroyl, alkoxycarbonyl, aryloxycarbonyl or heteroaryloxycarbonyl;  $R_2$  and  $R_3$  are each hydrogen, or, taken together are  $:NR_4$ ;  $R_4$  is hydrogen,  $R_5O_2C$ ,  $HO$ , cyano,  $R_5CO$ ,  $HCO$ , lower alkyl, nitro, etc.;  $R_5$  is alkyl, aryl, heteroaryl, aralkyl, or heteroaralkyl;  $L_1$  is alkylene, alkenylene or alkynylene;  $L_2$  is absent, alkylene, alkenylene, alkynylene, alkylene-O, alkenylene-O, etc., provided that when  $L_2$  is absent, then  $R$  is not hydrogen, and  $Q$  is attached to  $R$  through a carbon atom thereof;  $Q$  is  $NR_8'$ ,  $O$ ,  $CO$ ,  $CO_2$ ,  $O_2C$ ,  $NR_8'(X_1)$ ,  $C(X)NR_8'$ ,  $NR_8C(X_1)O$ , etc.; provided that a nitrogen atom or oxygen atom of  $Q$  is not directly bonded to a carbon atom of  $L_1$  or  $L_2$  having a double bond or triple bond, or  $Q-L_2-R$  is cycloalkyl, cycloalkenyl, heterocyclyl, fused arylcycloalkyl, fused heteroaryl cycloalkyl, etc.; provided that a nitrogen atom or oxygen atom of  $Q$  is not directly bonded to a carbon atom of  $L_1$  having a double bond or triple bond;  $X_1$  is  $O$  or  $S$ ;  $R_8'$  is hydrogen, alkyl, aralkyl, heteroaralkyl, acyl, aroyl, heteroaroyl or alkoxycarbonyl;  $R_8$  is hydrogen, alkyl, aralkyl, heteroaralkyl, acyl, aroyl or heteroaroyl; and  $m$  is  $0$ ,  $1$  or  $2$ ], oxides thereof, pharmaceutically acceptable salts, solvates thereof, or prodrugs thereof are prepd. These compds. inhibit the formation of simultaneously directly inhibiting both Factor Xa and Factor IIa (thrombin) and are useful for treating pathol. conditions in a patient that may be ameliorated by administration of such compds. The pathol. conditions include venous vasculature, arterial vasculature, abnormal thrombus formation, acute myocardial infarction, unstable angina, thromboembolism, acute vessel closure assocd. with thrombolytic therapy, percutaneous transluminal coronary angioplasty, transient ischemic attacks, stroke, intermittent claudication or bypass grafting of the coronary or peripheral arteries, vessel luminal narrowing, restenosis post coronary or venous angioplasty, maintenance of vascular access patency in longterm hemodialysis patients, pathol. thrombus formation occurring in the veins of the lower extremities following abdominal, knee and hip surgery, a risk of pulmonary thromboembolism, or disseminated systemic intravascular coagulopathy occurring in vascular systems during septic shock, certain viral infections or cancer (no data). Thus, To a cooled ( $0^\circ$  degree.) soln. of 5-(pyrid-2-yl)thiophene-2-carboxylic acid and 4-methylmorpholine in  $CH_2Cl_2$  is added dropwise a soln. of iso-Pr chloroformate in toluene, stirred 30 min, treated with 2-[5-(N-tert-butoxycarbonyl)carbamimidoyl-2,3-dihydrobenzofuran-3-



yl]ethylamine in DMF, and the reaction mixt. was allowed to warm to room temp. overnight to give 5-pyridin-2-ylthiophene-2-carboxylic acid [2-[5-(N-tert-butoxycarbonyl)carbamimidoyl-2,3-dihydrobenzofuran-3-yl]ethyl]amide which was stirred with H<sub>2</sub>O and CF<sub>3</sub>CO<sub>2</sub>H in CH<sub>2</sub>Cl<sub>2</sub> for 3 h to give 5-(pyridin-2-yl)thiophene-2-carboxylic acid [2-(5-carbamimidoyl-2,3-dihydrobenzofuran-3-yl)ethyl]amide.

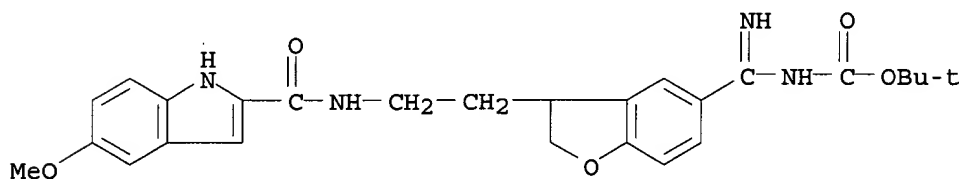
IT 328124-89-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and -benzopyrans as inhibitors of factor Xa and factor IIa)

RN 328124-89-6 HCAPLUS

CN Carbamic acid, [[2,3-dihydro-3-[2-[[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]ethyl]-5-benzofuranyl]iminomethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



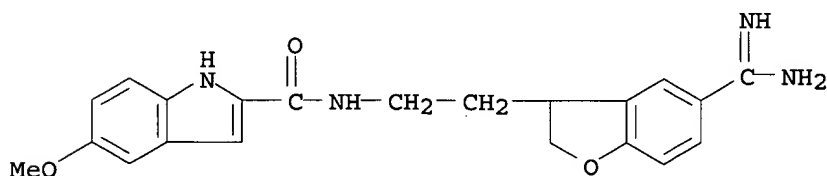
IT 328124-08-9P 328124-37-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted (aminoiminomethyl or aminomethyl)dihydrobenzofurans and -benzopyrans as inhibitors of factor Xa and factor IIa)

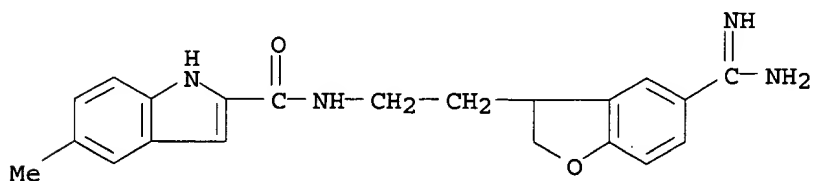
RN 328124-08-9 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[5-(aminoiminomethyl)-2,3-dihydro-3-benzofuranyl]ethyl]-5-methoxy- (9CI) (CA INDEX NAME)

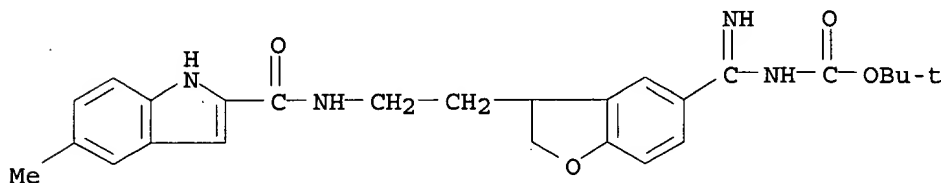


RN 328124-37-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[5-(aminoiminomethyl)-2,3-dihydro-3-benzofuranyl]ethyl]-5-methyl- (9CI) (CA INDEX NAME)



IT 328124-64-7P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of substituted (aminoiminomethyl or aminomethyl) dihydrobenzofurans and -benzopyrans as inhibitors of factor Xa and factor IIa)  
 RN 328124-64-7 HCAPLUS  
 CN Carbamic acid, [[2,3-dihydro-3-[2-[[[(5-methyl-1H-indol-2-yl)carbonyl]amino]ethyl]-5-benzofuranyl]iminomethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L31 ANSWER 15 OF 30 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 2000:573516 HCAPLUS  
 DOCUMENT NUMBER: 133:168404  
 TITLE: Osmotic system for delivery of solid amorphous dispersions of drugs  
 INVENTOR(S): Appel, Leah Elizabeth; Curatolo, William John; Herbig, Scott Max; Nightingale, James Alan Schriver; Thombre, Avinash Govind  
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA  
 SOURCE: Eur. Pat. Appl., 29 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1027888	A2	20000816	EP 2000-300572	20000126
EP 1027888	A3	20010228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2000229846	A2	20000822	JP 2000-33132	20000210
BR 2000000358	A	20010821	BR 2000-358	20000210
PRIORITY APPLN. INFO.:			US 1999-119406P P 19990210	

AB Controlled release dosage forms for low soly. drugs comprise an amorphous solid dispersion of the drug coated with a non-dissolving and non-eroding coating that controls the influx of water to the core so as to cause extrusion of a portion of the core, as well as a method of treating a disease or disorder comprising administering such dosage form to a person. A solid dispersion was prepd. from [R-(R\*,S\*)]-5-chloro-N-[2-hydroxy-3-[methoxymethylamino-3-oxo-1-(phenylmethyl)propyl]propyl]-1H-indole-2-carboxamide (a **glycogen phosphorylase inhibitor**) and hydroxypropyl Me cellulose acetate succinate.

IT 9035-74-9, Glycogen phosphorylase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; osmotic system for delivery of solid amorphous dispersions of drugs)

RN 9035-74-9 HCAPLUS  
CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

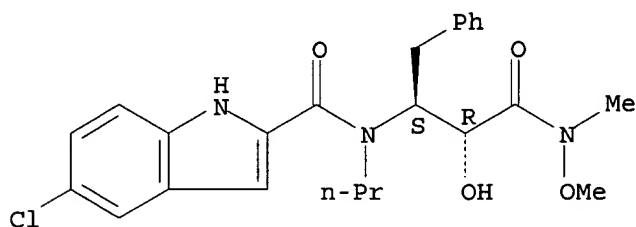
IT 288154-34-7 288154-35-8

RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)  
(osmotic system for delivery of solid amorphous dispersions of drugs)

RN 288154-34-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]-N-propyl- (9CI) (CA INDEX NAME)

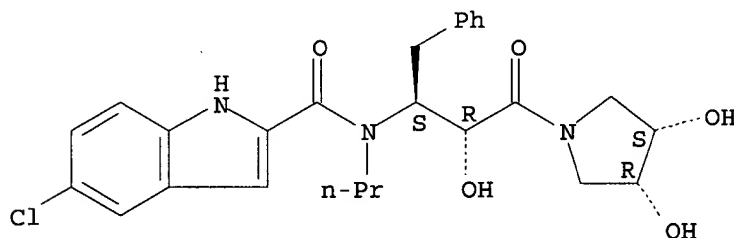
Absolute stereochemistry.



RN 288154-35-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-N-propyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:260225 HCAPLUS

DOCUMENT NUMBER: 132:294010

TITLE: Preparation of diaminopropionic acid derivatives as intracellular adhesion molecule-1 (ICAM-1) binding inhibitors

INVENTOR(S): Fotouhi, Nader; Gillespie, Paul; Guthrie, Robert William; Pietranico-Cole, Sherrie Lynn; Yun, Weiya

PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.

SOURCE: PCT Int. Appl., 259 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

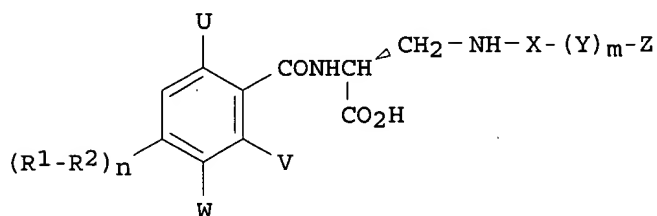
PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

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 WO 2000021920      A1      20000420      WO 1999-EP7620      19991012  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,  
 DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,  
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,  
 MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
 TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,  
 MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 US 6331640      B1      20011218      US 1999-407534      19990929  
 BR 9914602      A      20010703      BR 1999-14602      19991012  
 EP 1121342      A1      20010808      EP 1999-953772      19991012  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 JP 2002527416      T2      20020827      JP 2000-575829      19991012  
 US 2002052512      A1      20020502      US 2001-879700      20010612  
 PRIORITY APPLN. INFO.:      US 1998-104120P      P      19981013  
    US 1999-407534      A3      19990929  
    WO 1999-EP7620      W      19991012  
 OTHER SOURCE(S):      MARPAT 132:294010  
 GI



AB Diaminopropionic acid derivs. I [R1 = substituted 1-naphthyl, 4-indolyl, 4-benzimidazolyl, 4-benzodiazolyl, 4-benzotriazolyl, or phenyl; R2 = CHR3NHCO (R3 = H, carboxy, alkyl), CH2CH2CO, 1,2-cyclopropanediylcarbonyl, OCH2CO, CH:CHCHR3, CH2CH2CH(OH), CONHCHR3, or CH2NH-5,1-tetrazolediyl; U, V, W = H, halo, alkyl provided that U and V are not both hydrogen; X = CO, phenylalkylene, sulfonyl; Y = alkylene which may be substituted by amino or cycloalkyl, alkenylene, alkyleneithio; Z = H, alkylthio, CO2H, CONH2, 1-adamantyl, diphenylmethyl, 3-[[[(5-chloro-2-pyridinyl)amino]carbonyl]-2-pyrazinyl, hydroxy, phenylmethoxy, 2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]phenyl, [(2,6-dichlorophenyl)methoxy], Ph, (un)substituted cycloalkyl or aryl or fused ring system which may contain 0-3 heteroatoms; m, n = 0, 1] or their pharmaceutically acceptable salts or esters were prepd. and are useful for treating rheumatoid arthritis, psoriasis, multiple sclerosis, Crohn's disease, ulcerative colitis, atherosclerosis, restenosis, pancreatitis, transplant rejection, delayed graft function and diseases of **ischemia reperfusion** injury, including acute **myocardial** infarction and stroke. Thus, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-(3-methoxybenzoylamino)-L-alanine was prepd. by the solid-phase method and showed IC50 = 1.2 nM in the LFA-1 (lymphocyte function-assocd. antigen-1)/ICAM-1 protein-protein assay.

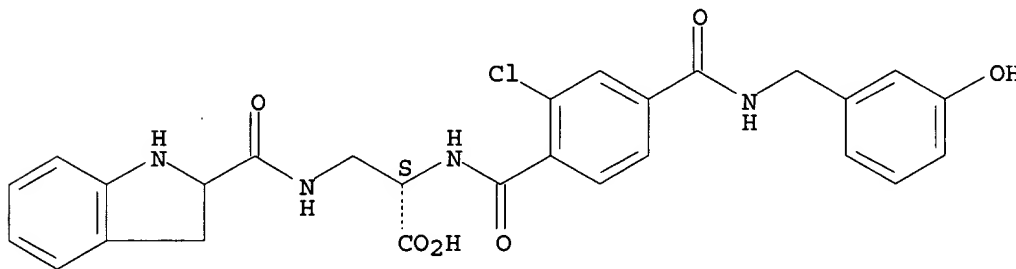
IT 264275-03-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of diaminopropionic acid derivs. as intracellular adhesion mol.-1 (ICAM-1) binding inhibitors)

RN 264275-03-8 HCAPLUS

CN L-Alanine, N-[2-chloro-4-[[[(3-hydroxyphenyl)methyl]amino]carbonyl]benzoyl]-3-[[[(2,3-dihydro-1H-indol-2-yl)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:98049 HCAPLUS

DOCUMENT NUMBER: 132:148495

TITLE: Preparation of **inhibitors** of human **glycogen phosphorylase** and their therapeutical applications

INVENTOR(S): Rath, Virginia Leigh; Hoover, Dennis Jay; Ammirati, Mark

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 42 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 978279	A1	20000209	EP 1999-306047	19990729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 2002031816	A1	20020314	US 1999-369214	19990805
JP 2000083662	A2	20000328	JP 1999-225128	19990809
BR 9903571	A	20010306	BR 1999-3571	19990809

PRIORITY APPLN. INFO.: US 1998-95790P P 19980807

OTHER SOURCE(S): MARPAT 132:148495

AB The present invention is directed to a novel binding site for a **glycogen phosphorylase inhibitor** found within a **glycogen phosphorylase** enzyme. The novel binding site allows the design of novel **glycogen phosphorylase inhibitors**. A method of treatment of hyperglycemia, hyperinsulinemia, hyperlipidemia, insulin resistance or tissue ischemia using the **glycogen phosphorylase inhibitor**

is disclosed.

IT 257624-03-6P

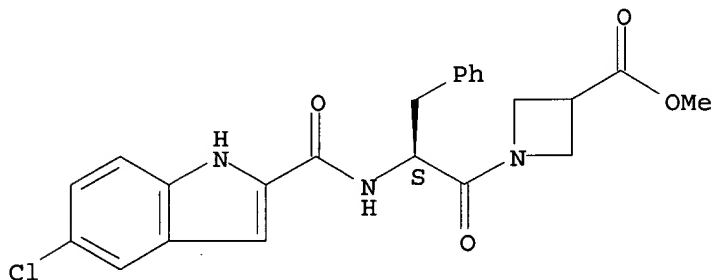
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of inhibitors of human glycogen phosphorylase and their therapeutical applications)

RN 257624-03-6 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(2S)-2-[[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-oxo-3-phenylpropyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 257624-04-7P 257624-05-8P

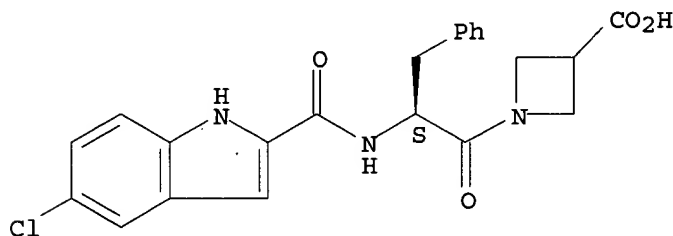
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of inhibitors of human glycogen phosphorylase and their therapeutical applications)

RN 257624-04-7 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(2S)-2-[[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-oxo-3-phenylpropyl]-, monosodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.

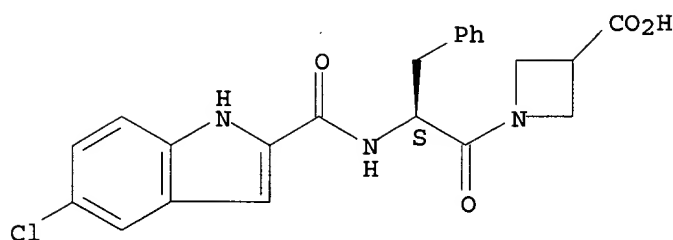


● Na

RN 257624-05-8 HCAPLUS

CN 3-Azetidinecarboxylic acid, 1-[(2S)-2-[[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-oxo-3-phenylpropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9035-74-9**, Glycogen phosphorylase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
 (prepn. of **inhibitors** of human glycogen phosphorylase and their therapeutical applications)  
 RN 9035-74-9 HCAPLUS  
 CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT **9035-74-9D**, Phosphorylase, **inhibitor** complexes  
 RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)  
 (prepn. of **inhibitors** of human glycogen phosphorylase and their therapeutical applications)  
 RN 9035-74-9 HCAPLUS  
 CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:15754 HCAPLUS

DOCUMENT NUMBER: 132:288599

TITLE: Pharmacological interference with hepatic glucose production

AUTHOR(S): Burger, H.-J.; Schubert, G.; Hemmerle, H.; Kramer, W.; Herling, A. W.

CORPORATE SOURCE: Hoechst Marion Roussel Deutschland GmbH, Frankfurt am Main, 65926, Germany

SOURCE: Annals of the New York Academy of Sciences (1999), 892 (Metabolic Syndrome X), 312-314  
 CODEN: ANYAA9; ISSN: 0077-8923

PUBLISHER: New York Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The present study was designed to characterize different pharmacol. approaches to interfere with hepatic glucose prodn. It can be concluded that the best way to reduce hepatic glucose prodn. is the inhibition of hepatic glucose-6- phosphatase activity. Pharmacol. approaches to reduce hepatic glucose prodn. are rational objectives for type 2 **diabetes** therapy.

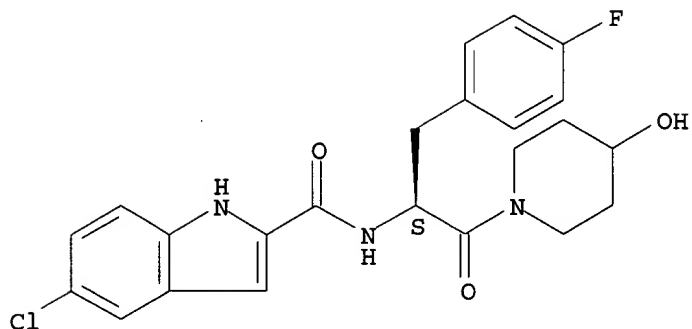
IT **186430-23-9**, CP 320626

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (pharmacol. interference with hepatic glucose prodn.)

RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidiny)-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:613914 HCAPLUS

DOCUMENT NUMBER: 131:257875

TITLE: Preparation of heterocyclcyl phosphotyrosine derivatives as SH2-mediated signal transduction inhibitors

INVENTOR(S): Buchanan, John; Bohacek, Regine; Vu, Chi B.; Luke, George P.

PATENT ASSIGNEE(S): Ariad Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 194 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

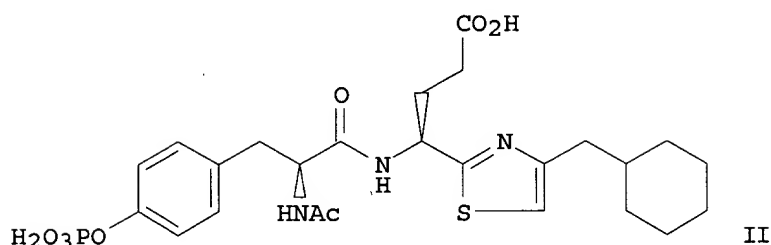
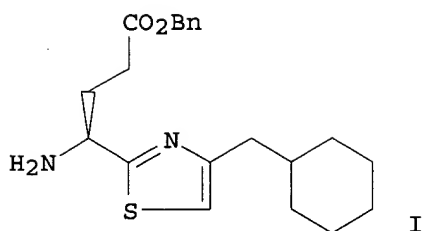
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947529	A1	19990923	WO 1999-US5970	19990318
W: CA, CZ, JP, MX, RU, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2319493	AA	19990923	CA 1999-2319493	19990318
EP 1064289	A1	20010103	EP 1999-912685	19990318
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002506873	T2	20020305	JP 2000-536724	19990318
PRIORITY APPLN. INFO.:			US 1998-78412P	P 19980318
			US 1998-108084P	P 19981112
			WO 1999-US5970	W 19990318
OTHER SOURCE(S):		MARPAT 131:257875		
GI				





AB Heterocyclic phosphotyrosine derivs. were prepd. for inhibiting intracellular signal transduction, esp. intracellular signal transduction mediated by a PDGF receptor protein, EGF receptor protein, HER2/Neu receptor protein, fibroblast growth factor receptor protein, focal adhesion kinase protein, p130 protein, or p68 protein. For example, BOC-Tyr(PO<sub>3</sub>Bn<sub>2</sub>)-OH (BOC = tert-butoxycarbonyl; Bn = benzyl) and the thiazolylamine salt (I).cntdot.TFA (four step prepn. given) were coupled, the phosphate deprotected, the amine acylated, and the carboxylic acid deprotected to form the title compd. (II). In an assay for binding affinities to Src SH2, thirteen compds. of the invention were detd. to have IC<sub>50</sub> values of < 50.mu.M. In an assay for binding affinities to Zap-70 SH2, fourteen compds. of the invention exhibited IC<sub>50</sub> values of < 50.mu.M. This invention also relates to pharmaceutical compns. contg. the compds. and prophylactic and therapeutic methods involving pharmaceutical and veterinary administration of the compds. for proliferative disease, cancer, restenosis, osteoporosis, inflammation, allergies, **cardiovascular** disease, or immunosuppression.

IT 244210-62-6P

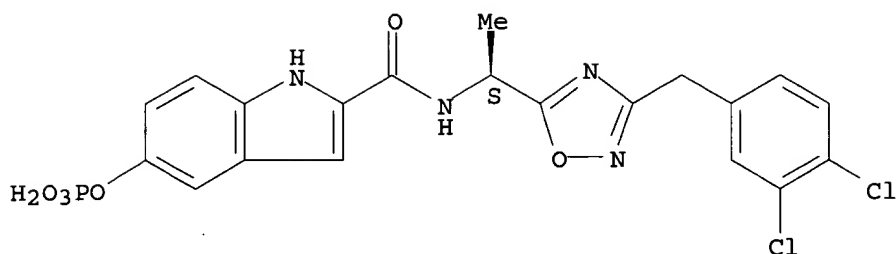
RL: **BAC (Biological activity or effector, except adverse)**; BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; prepn. of heterocyclyl phosphotyrosine derivs. as SH2-mediated signal transduction inhibitors)

RN 244210-62-6 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S)-1-[3-[(3,4-dichlorophenyl)methyl]-1,2,4-oxadiazol-5-yl]ethyl]-5-(phosphonooxy)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:354425 HCAPLUS

DOCUMENT NUMBER: 131:9635

TITLE: Combination of an aldose reductase inhibitor and a **glycogen phosphorylase inhibitor**

INVENTOR(S): Mylari, Banavara Lakshman; Hoover, Dennis Jay; Hulin, Bernard; Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9926659	A1	19990603	WO 1998-IB1752	19981102
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2310069	AA	19990603	CA 1998-2310069	19981102
AU 9895558	A1	19990615	AU 1998-95558	19981102
AU 733304	B2	20010510		
EP 1032424	A1	20000906	EP 1998-949193	19981102
EP 1032424	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
BR 9814698	A	20001003	BR 1998-14698	19981102
AT 205403	E	20010915	AT 1998-949193	19981102
ES 2161548	T3	20011201	ES 1998-949193	19981102
JP 2002504478	T2	20020212	JP 2000-521860	19981102
ZA 9810636	A	20000522	ZA 1998-10636	19981120
NO 2000002164	A	20000719	NO 2000-2164	20000427
PRIORITY APPLN. INFO.:			US 1997-66365P	P 19971121
			WO 1998-IB1752	W 19981102

AB Pharmaceutical compns., kits and methods comprising combination of aldose reductase inhibitors (0.1-20 mg/kg) and **glycogen phosphorylase inhibitors** (0.1-15 mg/kg), useful for treatment of insulin resistant conditions such as **diabetes**,

hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, and tissue ischemia, etc., are described. E.g., a tablet formulation contained an active ingredient (an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, or a combination of the two) 0.25-100, starch 45, microcryst. cellulose 35, PVP (as 10% soln. in water) 4, Na CM-cellulose 4.5, Mg stearate 0.5, and talc 1 mg/tablet, resp.

IT 186392-40-5 186392-43-8 186392-49-4  
186392-53-0 186392-64-3 186429-64-1  
186429-78-7 186430-11-5 186430-23-9  
186430-41-1 186430-52-4 186431-27-6  
208830-24-4 208830-25-5 225929-30-6

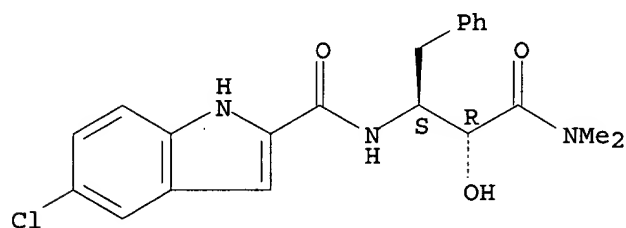
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(comps. for inhibitors of aldose reductase and glycogen phosphorylase for prevention and treatment of insulin resistant conditions in humans)

RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

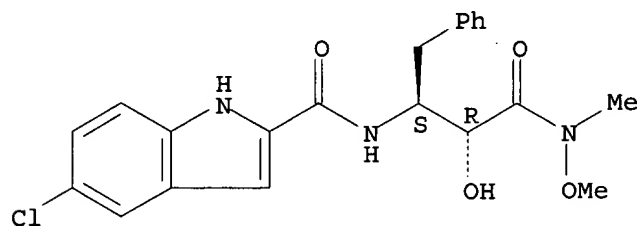
Absolute stereochemistry.



RN 186392-43-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

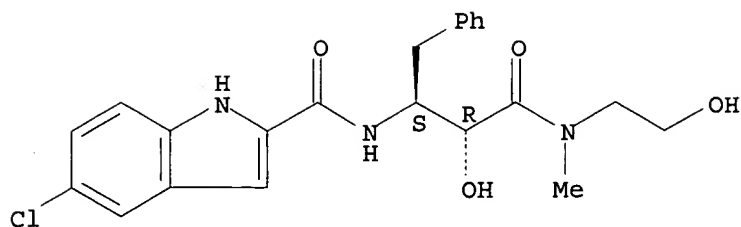
Absolute stereochemistry.



RN 186392-49-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

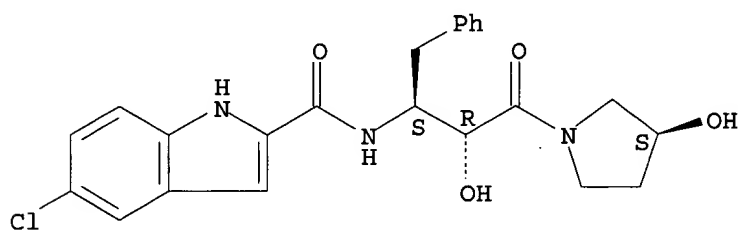
Absolute stereochemistry.



RN 186392-53-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

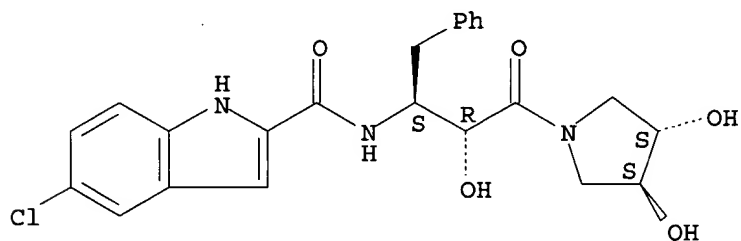
Absolute stereochemistry.



RN 186392-64-3 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

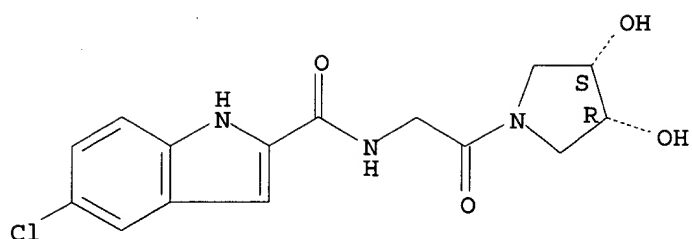
Absolute stereochemistry.



RN 186429-64-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3R,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]-, rel- (9CI) (CA INDEX NAME)

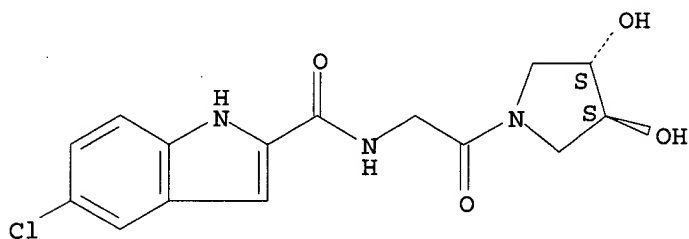
Relative stereochemistry.



RN 186429-78-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

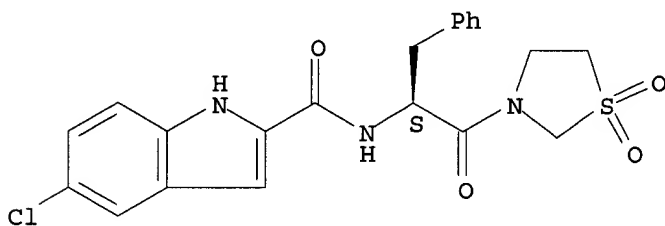
Absolute stereochemistry.



RN 186430-11-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(1,1-dioxido-3-thiazolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

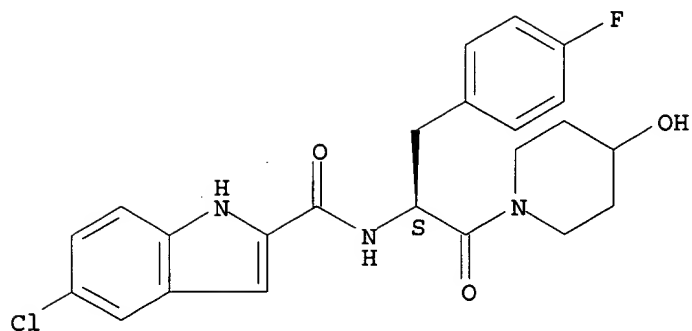
Absolute stereochemistry.



RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

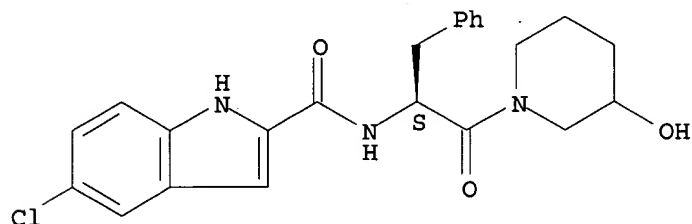
Absolute stereochemistry.



RN 186430-41-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-piperidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

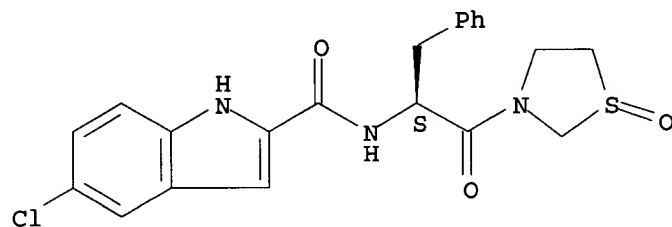
Absolute stereochemistry.



RN 186430-52-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(1-oxido-3-thiazolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

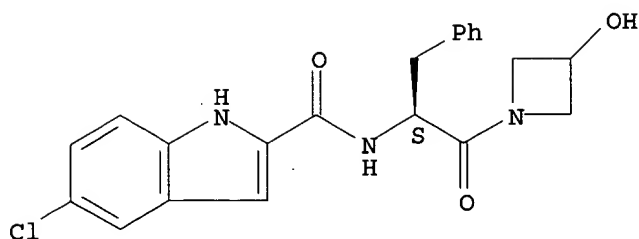
Absolute stereochemistry.



RN 186431-27-6 HCAPLUS

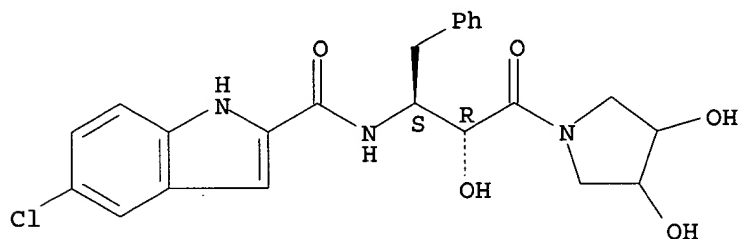
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidinyll)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



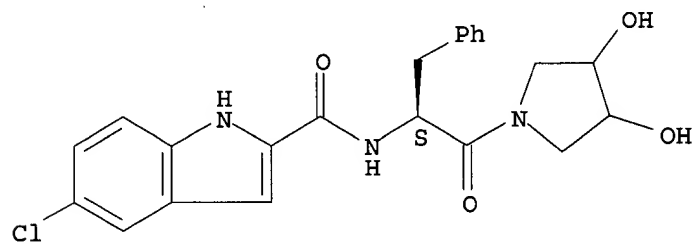
RN 208830-24-4 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



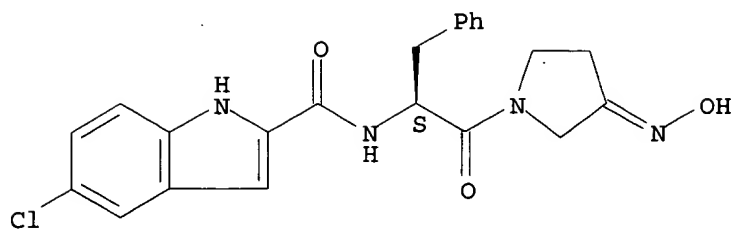
RN 208830-25-5 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3,4-dihydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 225929-30-6 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



IT 9035-74-9, Glycogen phosphorylase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
 (Biological study); PROC (Process)  
 (compns. for **inhibitors** of aldose reductase and glycogen  
 phosphorylase for prevention and treatment of insulin resistant  
 conditions in humans)  
 RN 9035-74-9 HCAPLUS  
 CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L31 ANSWER 21 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:450920 HCAPLUS

DOCUMENT NUMBER: 129:189205

TITLE: Indole-2-carboxamide **inhibitors** of human  
 liver **glycogen phosphorylase**

AUTHOR(S): Hoover, Dennis J.; Lefkowitz-Snow, Sheri;  
 Burgess-Henry, Jana L.; Martin, William H.; Armento,  
 Sandra J.; Stock, Ingrid A.; McPherson, R. Kirk;  
 Genereux, Paul E.; Gibbs, E. Michael; Treadway, Judith  
 L.

CORPORATE SOURCE: Department of Cardiovascular and Metabolic Diseases  
 Medicinal Chemistry, Central Research Division, Pfizer  
 Inc., Groton, CT, 06340, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(16),  
 2934-2938

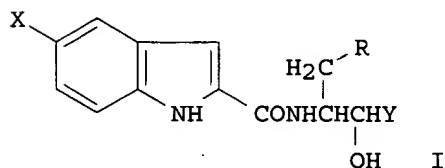
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB Indole-2-carboxamide derivs. (I; X = Cl, F, Br, H, OMe; R = Ph,  
 cyclohexyl, H, F; Y = CONMe<sub>2</sub>, CONHMe, CO<sub>2</sub>Me, CO<sub>2</sub>H, CH<sub>2</sub>OH, CONH<sub>2</sub>, etc.)  
 were prepd. I are potent **inhibitors** of human liver



**glycogen phosphorylase** which are active in cells, and produce hypoglycemic activity on oral administration in a rodent model of type 2 **diabetes**. I [CP-320626; X = Cl, R = F, Y = CO(1-piperidin-4-ol)] produced oral activity at 10 mg/kg.

IT 9035-74-9, Glycogen phosphorylase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)  
 (human liver; indole-2-carboxamide **inhibitors** of human liver glycogen phosphorylase)  
 RN 9035-74-9 HCAPLUS  
 CN Phosphorylase (9CI) (CA INDEX NAME)

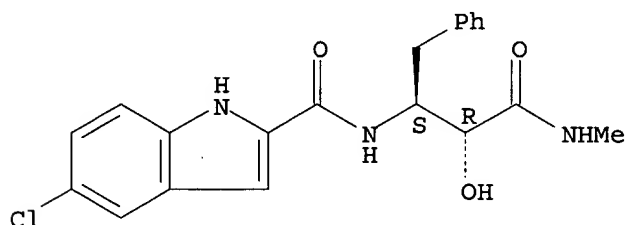
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 186392-10-9P 186392-11-0P 186392-12-1P  
 186392-13-2P 186392-22-3P 186392-32-5P  
 186392-33-6P 186392-34-7P 186392-38-1P  
 186392-40-5P 186392-56-3P 186429-59-4P  
 186429-60-7P 186430-05-7P 186430-23-9P  
 186430-32-0P 186430-34-2P 186430-36-4P  
 186430-37-5P 186430-39-7P 186430-44-4P  
 186432-25-7P 186432-26-8P 211677-10-0P  
 211677-11-1P 211677-12-2P 211677-13-3P  
 211677-14-4P 211677-15-5P 211677-16-6P  
 211677-17-7P 211677-18-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (indole-2-carboxamide inhibitors of human liver glycogen phosphorylase)

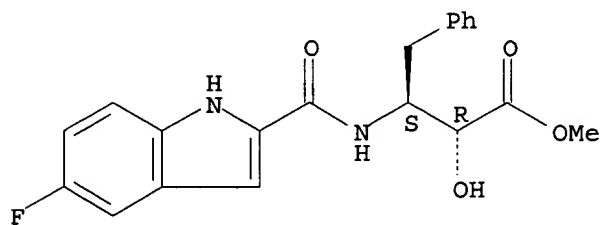
RN 186392-10-9 HCAPLUS  
 CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 186392-11-0 HCAPLUS  
 CN Benzenebutanoic acid, .beta.-[[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

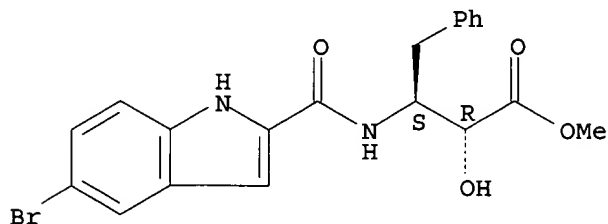
Absolute stereochemistry.



RN 186392-12-1 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[[5-bromo-1H-indol-2-yl)carbonyl]amino]-  
.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

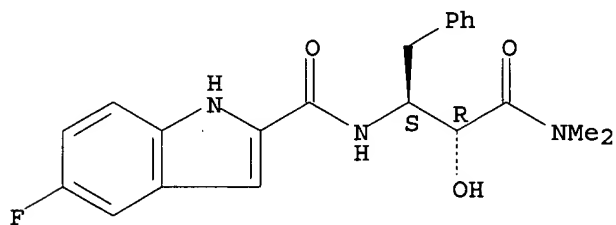
Absolute stereochemistry.



RN 186392-13-2 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-5-fluoro- (9CI) (CA INDEX NAME)

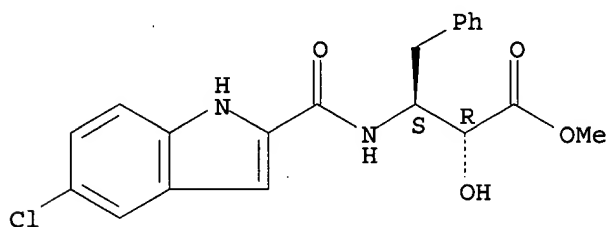
Absolute stereochemistry.



RN 186392-22-3 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[[5-chloro-1H-indol-2-yl)carbonyl]amino]-  
.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

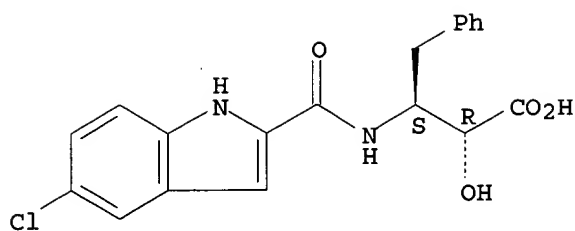
Absolute stereochemistry.



RN 186392-32-5 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[[5-chloro-1H-indol-2-yl)carbonyl]amino]-  
.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

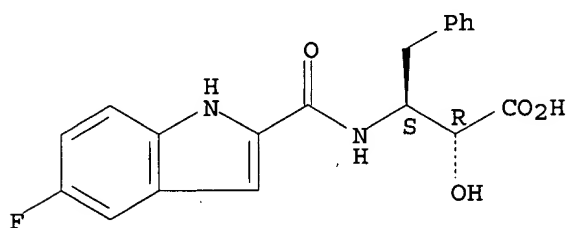
Absolute stereochemistry.



RN 186392-33-6 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-  
.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

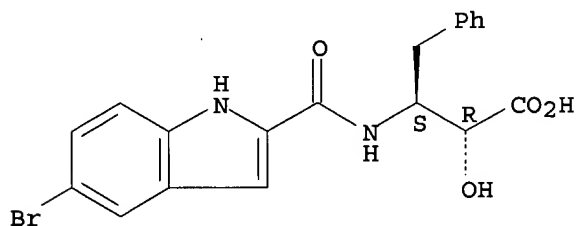
Absolute stereochemistry.



RN 186392-34-7 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[[(5-bromo-1H-indol-2-yl)carbonyl]amino]-  
.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

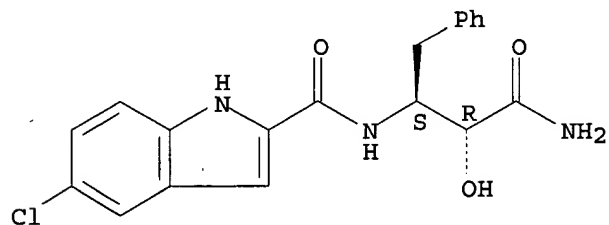
Absolute stereochemistry.



RN 186392-38-1 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S,2R)-3-amino-2-hydroxy-3-oxo-1-(  
(phenylmethyl)propyl)-5-chloro- (9CI) (CA INDEX NAME)

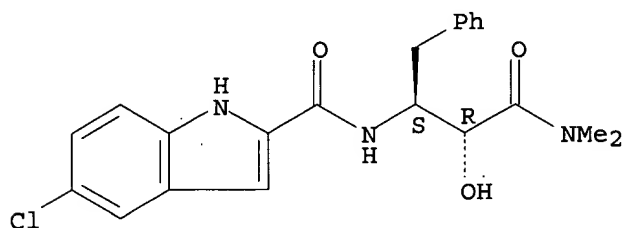
Absolute stereochemistry.



RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

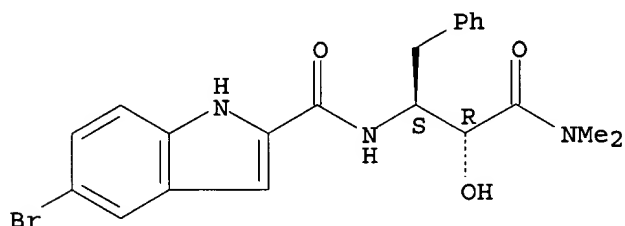
Absolute stereochemistry.



RN 186392-56-3 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-bromo-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

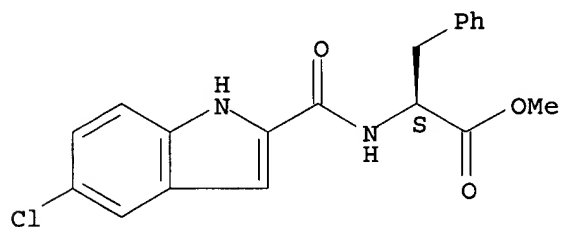
Absolute stereochemistry.



RN 186429-59-4 HCAPLUS

CN L-Phenylalanine, N-[(5-chloro-1H-indol-2-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

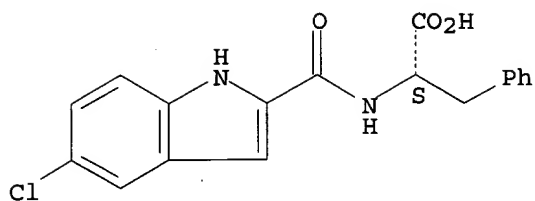
Absolute stereochemistry.



RN 186429-60-7 HCAPLUS

CN L-Phenylalanine, N-[(5-chloro-1H-indol-2-yl)carbonyl]- (9CI) (CA INDEX NAME)

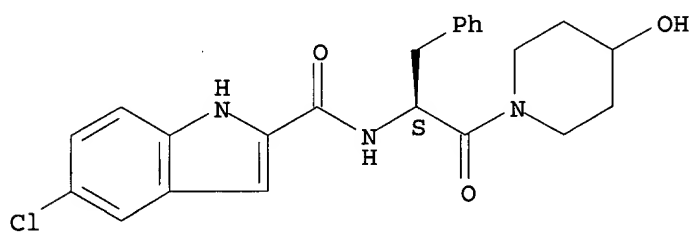
Absolute stereochemistry.



RN 186430-05-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(4-hydroxy-1-piperidiny)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

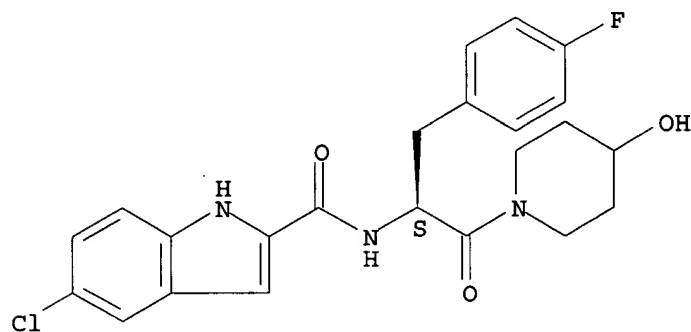
Absolute stereochemistry.



RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-hydroxy-1-piperidiny)-2-oxoethyl]- (9CI) (CA INDEX NAME)

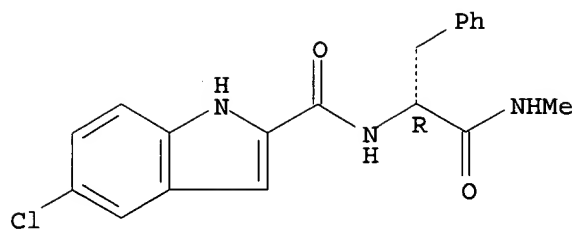
Absolute stereochemistry.



RN 186430-32-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

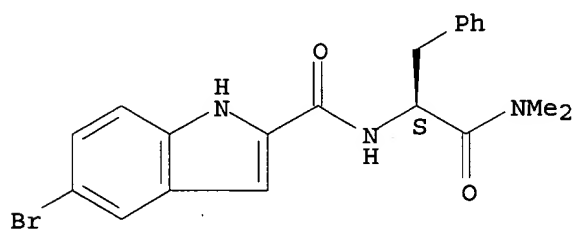
Absolute stereochemistry.



RN 186430-34-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-bromo-N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

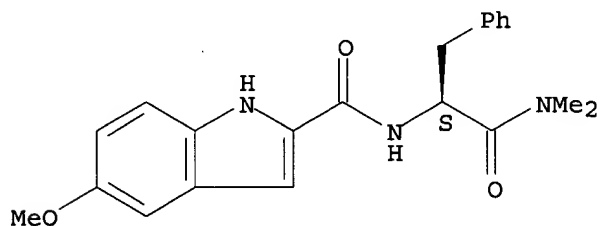
Absolute stereochemistry.



RN 186430-36-4 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-methoxy- (9CI) (CA INDEX NAME)

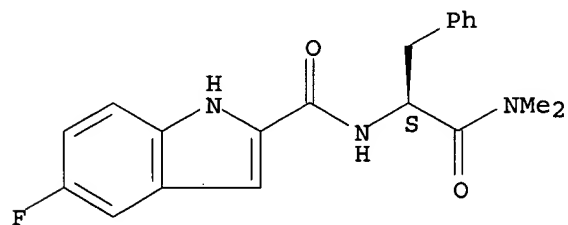
Absolute stereochemistry.



RN 186430-37-5 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]-5-fluoro- (9CI) (CA INDEX NAME)

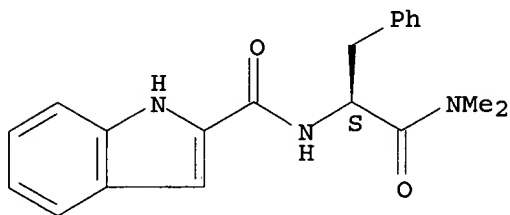
Absolute stereochemistry.



RN 186430-39-7 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

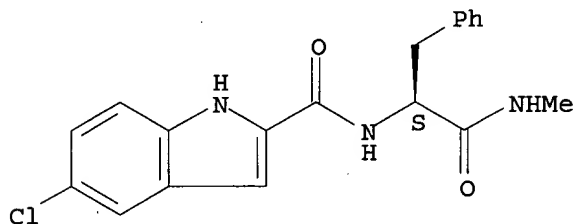
Absolute stereochemistry.



RN 186430-44-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(methylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

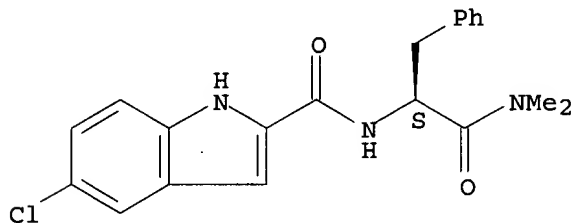
Absolute stereochemistry.



RN 186432-25-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

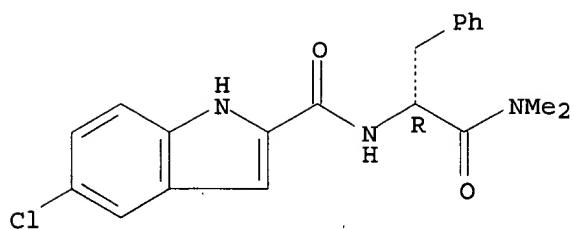
Absolute stereochemistry.



RN 186432-26-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

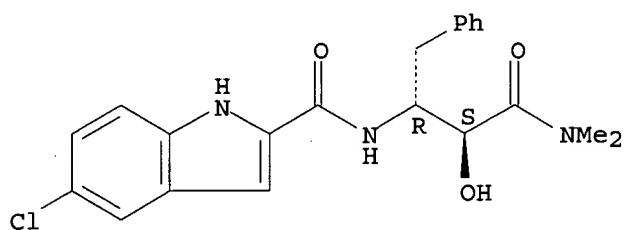
Absolute stereochemistry.



RN 211677-10-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2S)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

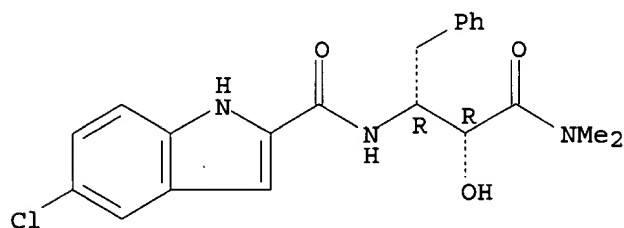
Absolute stereochemistry.



RN 211677-11-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

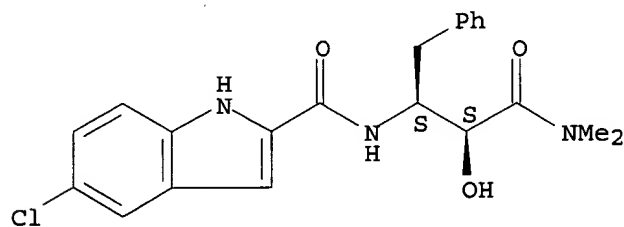
Absolute stereochemistry.



RN 211677-12-2 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2S)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

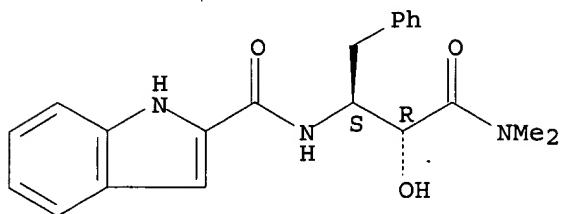


RN 211677-13-3 HCAPLUS



CN 1H-Indole-2-carboxamide, N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

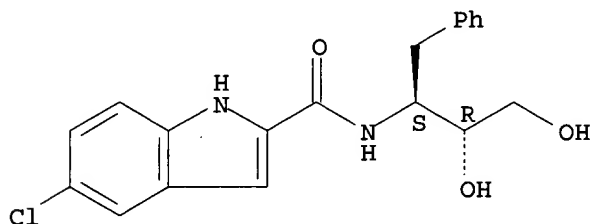
Absolute stereochemistry.



RN 211677-14-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2,3-dihydroxy-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

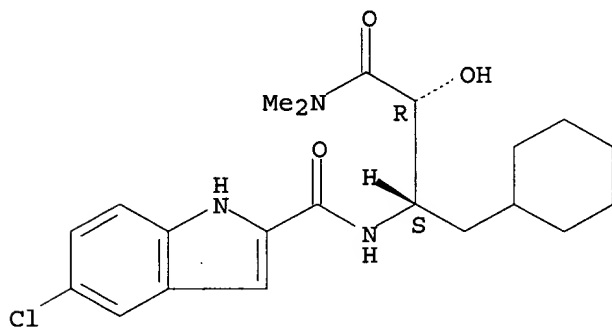
Absolute stereochemistry.



RN 211677-15-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-1-(cyclohexylmethyl)-3-(dimethylamino)-2-hydroxy-3-oxopropyl]- (9CI) (CA INDEX NAME)

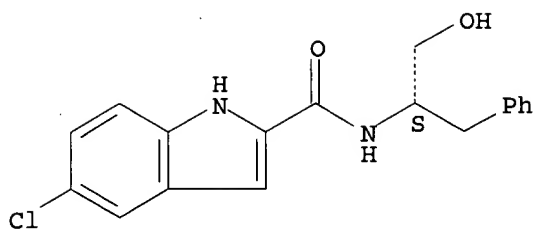
Absolute stereochemistry.



RN 211677-16-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-(hydroxymethyl)-2-phenylethyl]- (9CI) (CA INDEX NAME)

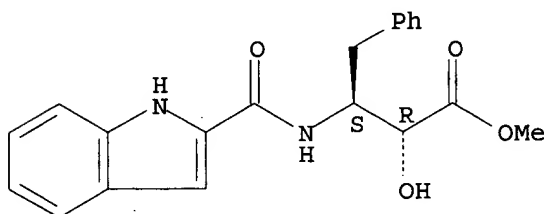
Absolute stereochemistry.



RN 211677-17-7 HCAPLUS

CN Benzenebutanoic acid, .alpha.-hydroxy-.beta.-[(1H-indol-2-ylcarbonyl)amino]-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

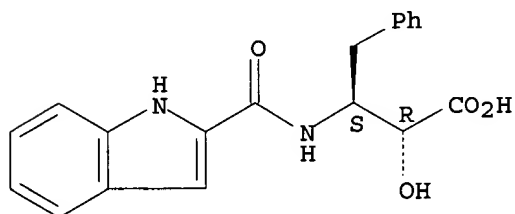
Absolute stereochemistry.



RN 211677-18-8 HCAPLUS

CN Benzenebutanoic acid, .alpha.-hydroxy-.beta.-[(1H-indol-2-ylcarbonyl)amino]-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:388320 HCAPLUS

DOCUMENT NUMBER: 129:72196

TITLE: Use of **glycogen phosphorylase inhibitor** for reducing non-cardiac tissue damage resulting from ischemia

INVENTOR(S): Hoover, Dennis J.; Martin, William Holt; Tracey, Wayne Ross; Treadway, Judith Lee

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: Eur. Pat. Appl., 52 pp.

CODEN: EPXXDW

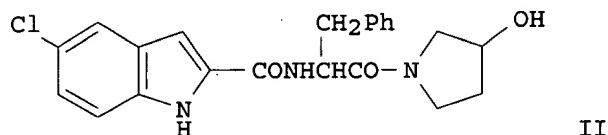
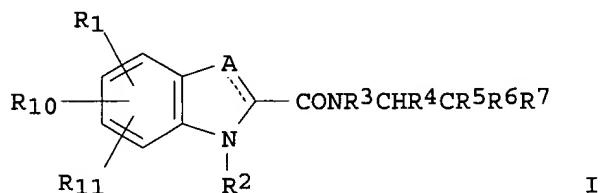
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 846464	A2	19980610	EP 1997-309727	19971203
EP 846464	A3	19990217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 5952322	A	19990914	US 1997-978384	19971125
CA 2223317	AA	19980605	CA 1997-2223317	19971203
JP 10194990	A2	19980728	JP 1997-332523	19971203
JP 3277147	B2	20020422		
AU 9746869	A1	19980611	AU 1997-46869	19971204
AU 717547	B2	20000330		
ZA 9710907	A	19990604	ZA 1997-10907	19971204
PRIORITY APPLN. INFO.:			US 1996-31584P	P 19961205
OTHER SOURCE(S):		MARPAT 129:72196		
GI				



AB The use of a **glycogen phosphorylase inhibitor** for the manuf. of a medicament for reducing non-cardiac tissue damage resulting from ischemia or hypoxia. The tissue is brain, liver, kidney, lung, gut, skeletal muscle, spleen, pancreas, nerve, spinal cord, retina tissue, the vasculature or intestinal tissue. Said **glycogen phosphorylase inhibitor** is represented by a compd. of formula [I; A = C(X): (wherein X = H, C1-4 alkyl, halo) when the dotted line is a bond; A = CH2 or CH(C1-4 alkyl) when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6-, or 7-NO2, cyano, C1-4 alkyl or alkoxy, CH2F, CF2H, CF3; R2 = H; R3 = H, C1-5 alkyl; R4 = H, Me, Et, n-Pr, C1-3 hydroxyalkyl, C1-3 alkoxy-C1-3 alkyl, phenyl-C1-4 alkyl, thien-2- or -3-yl-C1-4 alkyl, furan-2- or -3-yl-C1-4 alkyl, etc.; R5 = H, OH, F, C1-5 alkyl or alkoxy, C1-6 alkanoyl, amino-C1-4 alkoxy, mono-N- or di-N, N-C1-4 alkyl amino-C1-4 alkoxy, carboxy-C1-4 alkoxy, etc.; R7 = H, F, C1-5 alkyl; or R5 and R7 are taken together to form oxo; R6 = CO2H, C1-8 alkoxycarbonyl, (un)substituted CONH2, COR12; wherein R12 = piperazin-1-yl, 4-(C1-4 alkyl)piperazin-1-yl, 4-formylpiperazin-1-yl, morpholino, thiomorpholino, 1-oxothiomorpholino, 1,1-dioxothiomorpholino, thiazolidin-3-yl, etc.], e.g. indolecarboxamide (II) which **inhibited human liver glycogen phosphorylase a (HLGPa) and human muscle glycogen phosphorylase a (HMGPa) with IC50 of 45 and 85 nM, resp.**

IT 186392-40-5 186392-43-8 186392-46-1  
 186392-49-4 186392-53-0 186392-64-3  
 186429-66-3 186430-04-6 186430-23-9  
 186430-40-0 186431-27-6 186431-28-7  
 208830-24-4 208830-25-5

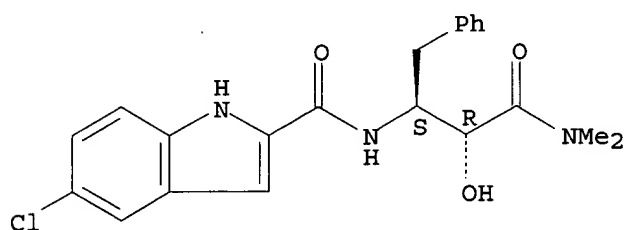
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(use of glycogen phosphorylase inhibitor for reducing non-cardiac tissue damage resulting from ischemia or hypoxia)

RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

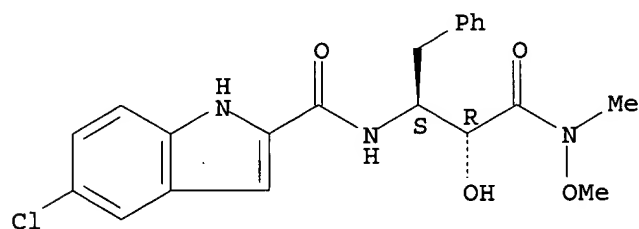
Absolute stereochemistry.



RN 186392-43-8 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(methoxymethylamino)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

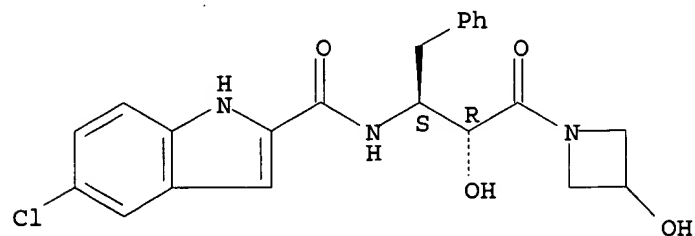
Absolute stereochemistry.



RN 186392-46-1 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-(3-hydroxy-1-azetidiny)-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

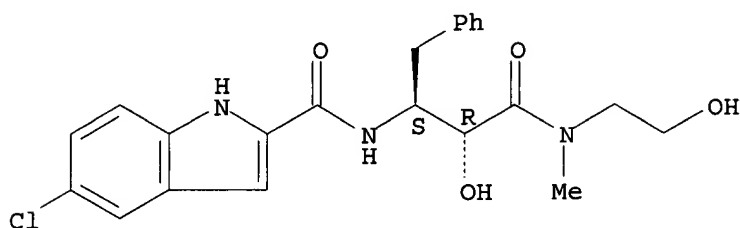


RN 186392-49-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(2-

hydroxyethyl)methylamino]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

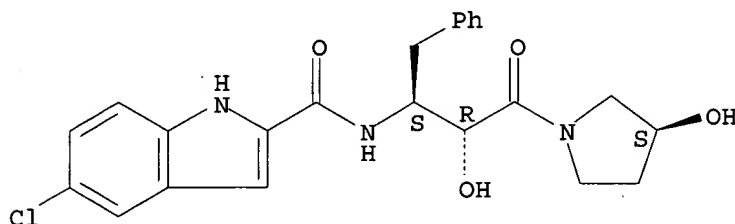
Absolute stereochemistry.



RN 186392-53-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-2-hydroxy-3-[(3S)-3-hydroxy-1-pyrrolidinyl]-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

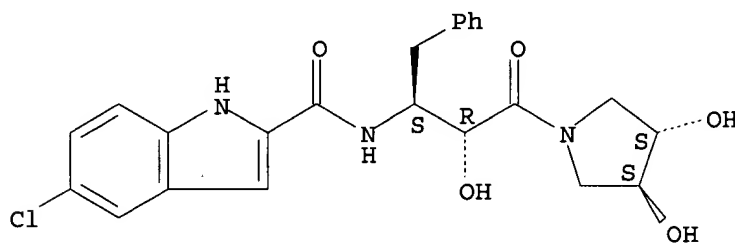
Absolute stereochemistry.



RN 186392-64-3 HCAPLUS

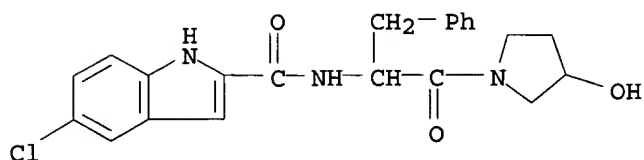
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-[(3S,4S)-3,4-dihydroxy-1-pyrrolidinyl]-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



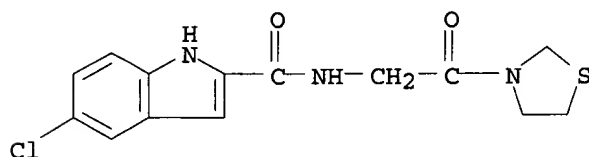
RN 186429-66-3 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-(3-hydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)



RN 186430-04-6 HCAPLUS

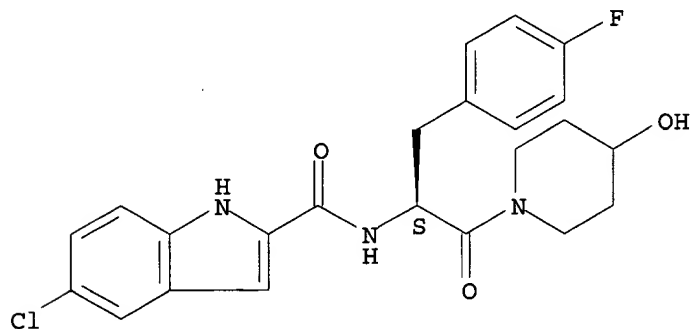
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2-oxo-2-(3-thiazolidinyl)ethyl]-  
(9CI) (CA INDEX NAME)



RN 186430-23-9 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-1-[(4-fluorophenyl)methyl]-2-(4-  
hydroxy-1-piperidinyl)-2-oxoethyl]- (9CI) (CA INDEX NAME)

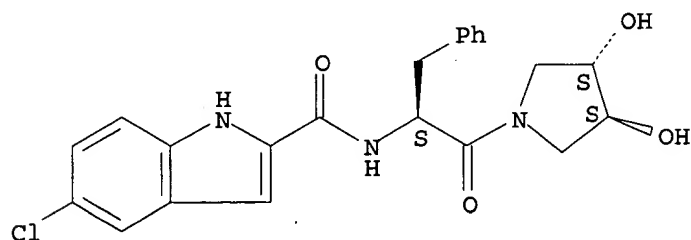
Absolute stereochemistry.



RN 186430-40-0 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[(3S,4S)-3,4-dihydroxy-1-  
pyrrolidinyl]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

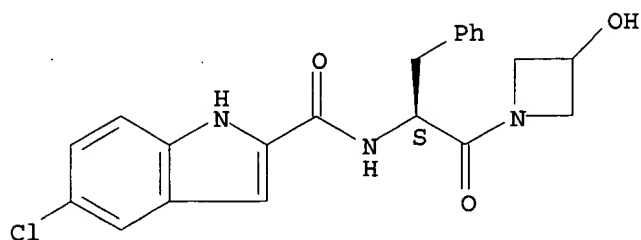
Absolute stereochemistry.



RN 186431-27-6 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3-hydroxy-1-azetidiny)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

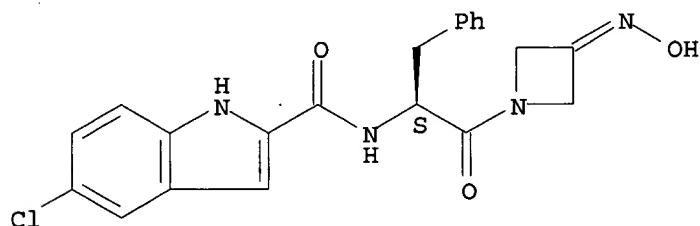
Absolute stereochemistry.



RN 186431-28-7 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-[3-(hydroxyimino)-1-azetidiny]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

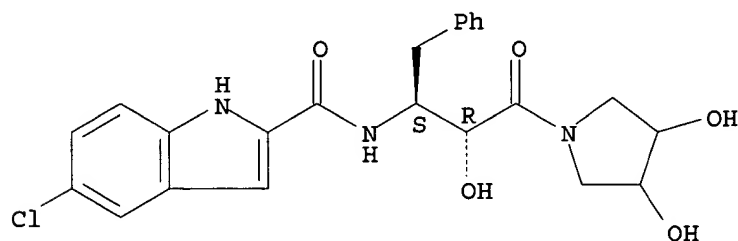
Absolute stereochemistry.



RN 208830-24-4 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(3,4-dihydroxy-1-pyrrolidinyl)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

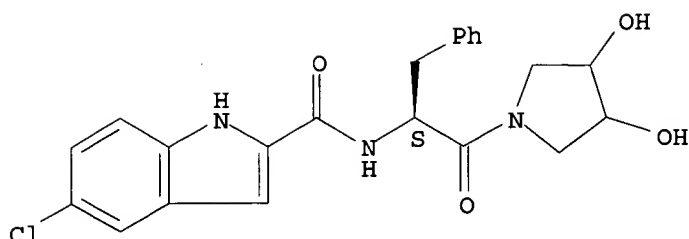
Absolute stereochemistry.



RN 208830-25-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S)-2-(3,4-dihydroxy-1-pyrrolidinyl)-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT **9035-74-9**, Glycogen phosphorylase  
 RL: BPR (Biological process); BSU (Biological study, unclassified); MSC  
 (Miscellaneous); BIOL (Biological study); PROC (Process)  
 (use of glycogen phosphorylase **inhibitor** for reducing  
 non-cardiac tissue damage resulting from ischemia or hypoxia)  
 RN 9035-74-9 HCAPLUS  
 CN Phosphorylase (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L31 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:197402 HCAPLUS

DOCUMENT NUMBER: 128:275085

TITLE: Combination therapy for reducing the risks associated  
 with **cardiovascular** disease

INVENTOR(S): Gould, Robert J.; Nichtberger, Steven A.; Rhymer,  
 Patricia A.; Olofsson, Lars

PATENT ASSIGNEE(S): Merck & Co., Inc., USA; Gould, Robert J.; Nichtberger,  
 Steven A.; Rhymer, Patricia A.; Olofsson, Lars

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811896	A1	19980326	WO 1997-US16388	19970915
W:	AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9743508	A1	19980414	AU 1997-43508	19970915
AU 723315	B2	20000824		
EP 946178	A1	19991006	EP 1997-941644	19970915
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
JP 2001500875	T2	20010123	JP 1998-514815	19970915
US 6251852	B1	20010626	US 1997-929595	19970915
US 6235706	B1	20010522	US 1999-147858	19990527
US 2001036913	A1	20011101	US 2001-764511	20010118
US 6403571	B2	20020611		

PRIORITY APPLN. INFO.:

US 1996-26581P P 19960918

GB 1996-21970 A 19961022

WO 1997-US16388 W 19970915



US 1999-147858 A3 19990527

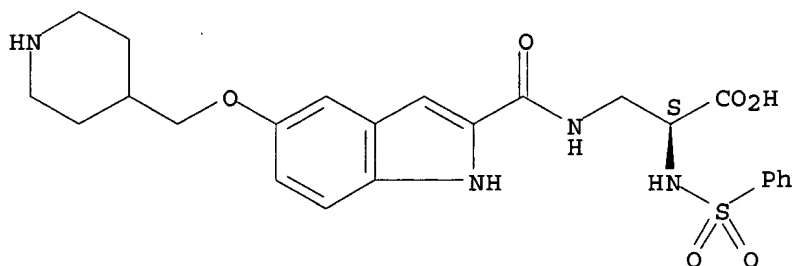
AB The instant invention involves a combination therapy and pharmaceutical compns. comprised of a therapeutically effective amt. of a cholesterol reducing agent such as an HMG-CoA reductase inhibitor in combination with a platelet aggregation inhibitor which is useful for inhibiting platelet aggregation, for inhibiting the formation of thrombotic occlusions, and for treating, preventing and reducing the risk of occurrence of **cardiovascular** and cerebrovascular events and related vaso-occlusive disorders. Tablets were prepd. contg. simvastatin and a glycoprotein IIb/IIIa receptor antagonist.

IT 190261-01-9  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (combination therapy for reducing the risks assocd. with cardiovascular disease)

RN 190261-01-9 HCAPLUS

CN L-Alanine, N-(phenylsulfonyl)-3-[[[5-(4-piperidinylmethoxy)-1H-indol-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:121995 HCAPLUS

DOCUMENT NUMBER: 128:252809

TITLE: Discovery of a human liver **glycogen phosphorylase inhibitor** that lowers blood glucose in vivo

AUTHOR(S): Martin, William H.; Hoover, Dennis J.; Armento, Sandra J.; Stock, Ingrid A.; Mcpherson, R. Kirk; Danley, Dennis E.; Stevenson, Ralph W.; Barrett, Eugene J.; Treadway, Judith L.

CORPORATE SOURCE: Central Research Division, Department of Exploratory Medicinal Biology, Pfizer, Inc, Groton, CT, 06340, USA

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(4), 1776-1781

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An **inhibitor** of human liver **glycogen phosphorylase a** (HLGPa) has been identified and characterized in vitro and in vivo. This substance, [R-(R\*,S\*)]-5-chloro-N-[3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]-1H-indole-2-carboxamide (CP-91149), inhibited HLGPa with an IC50 of 0.13 .mu.M in the presence of 7.5 mM glucose. CP-91149 resembles caffeine, a known allosteric phosphorylase inhibitor, in that it is 5- to 10-fold less potent in the absence of glucose. Further anal., however, suggests that CP-91149 and caffeine are kinetically distinct. Functionally, CP-91149

inhibited glucagon-stimulated glycogenolysis in isolated rat hepatocytes ( $P < 0.05$  at 10-100  $\mu\text{M}$ ) and in primary human hepatocytes (2.1  $\mu\text{M}$  IC<sub>50</sub>). In vivo, oral administration of CP-91149 to **diabetic** ob/ob mice at 25-50 mg/kg resulted in rapid (3 h) glucose lowering by 100-120 mg/dL ( $P < 0.001$ ) without producing hypoglycemia. Further, CP-91149 treatment did not lower glucose levels in normoglycemic, nondiabetic mice. In ob/ob mice pretreated with <sup>14</sup>C-glucose to label liver glycogen, CP-91149 administration reduced <sup>14</sup>C-glycogen breakdown, confirming that glucose lowering resulted from inhibition of glycogenolysis in vivo. These findings support the use of CP-91149 in investigating glycogenolytic vs. gluconeogenic flux in hepatic glucose prodn., and they demonstrate that glycogenolysis inhibitors may be useful in the treatment of type 2 **diabetes**.

IT 186392-40-5P, CP 91149

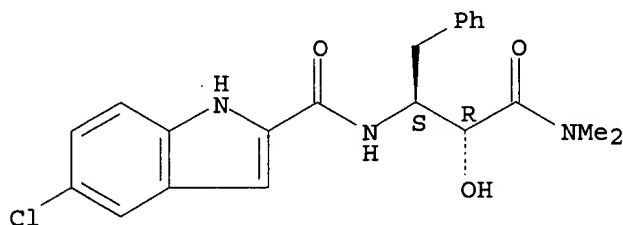
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

RN 186392-40-5 HCAPLUS

CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2R)-3-(dimethylamino)-2-hydroxy-3-oxo-1-(phenylmethyl)propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 186392-22-3P 186392-32-5P

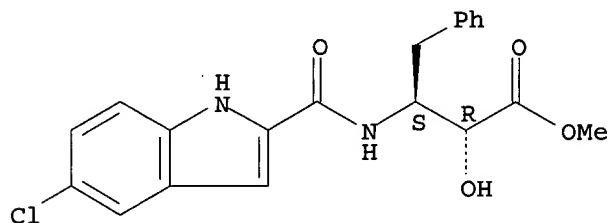
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(blood glucose lowering by CP-91149, oral inhibitor of human liver glycogen phosphorylase, in model of type II diabetes)

RN 186392-22-3 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, methyl ester, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

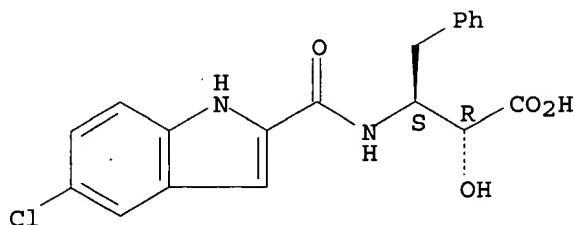
Absolute stereochemistry.



RN 186392-32-5 HCAPLUS

CN Benzenebutanoic acid, .beta.-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-.alpha.-hydroxy-, (.alpha.R,.beta.S)- (9CI) (CA INDEX NAME)

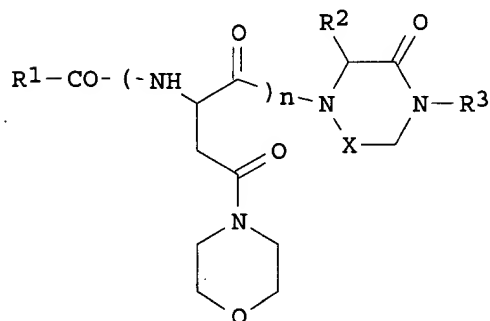
Absolute stereochemistry.



L31 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1998:115888 HCAPLUS  
 DOCUMENT NUMBER: 128:230390  
 TITLE: Preparation of piperazine derivatives as NO producing inhibitors  
 INVENTOR(S): Ito, Yoshikuni; Yatabe, Isao; Inoue, Takayuki; Hamashima, Hitoshi  
 PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10045751	A2	19980217	JP 1997-131796	19970522
PRIORITY APPLN. INFO.: AU 1996-83			19960527	
OTHER SOURCE(S): MARPAT 128:230390				

GI



I

AB The title compds. [I; R1 = indolyl, benzofuranyl; R2, R3 = (un)substituted alkyl, aryl, etc.; X = CH2, CO; n = 0, 1] are prepd. I, possessing NO producing inhibitory activity, are useful for prevention and treatment of brain infarction, Alzheimer disease, heart failure, diabetes and related diseases. Thus, (S)-I (R1 = 2-indolyl, R2 = CH2C6H5, R3 = Me, X = CH2, n = 1) is prepd. and showed 70.9% inhibitory activity at 10<sup>-5</sup> M for mouse RAW264.7 cell.

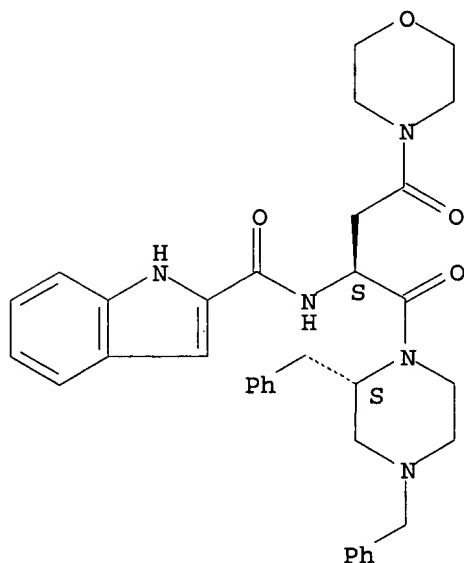
IT 204328-01-8P 204328-04-1P 204328-07-4P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);  
 BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of piperazine derivs. as NO producing inhibitors)

RN 204328-01-8 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[1-[[2,4-bis(phenylmethyl)-1-piperazinyl]carbonyl]-3-(4-morpholinyl)-3-oxopropyl]-, [S-(R\*,R\*)]- (9CI)  
 (CA INDEX NAME)

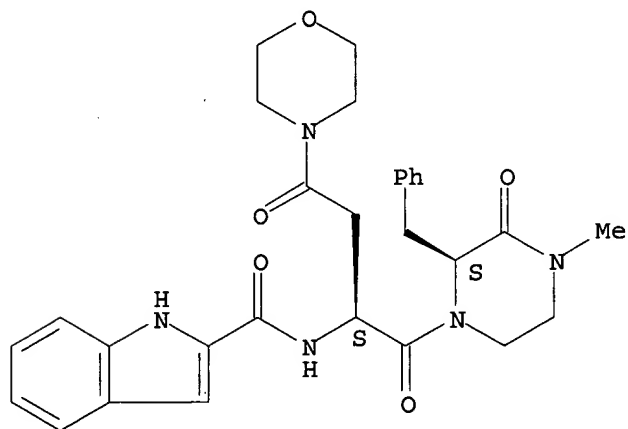
Absolute stereochemistry.



RN 204328-04-1 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[1-[[4-methyl-3-oxo-2-(phenylmethyl)-1-piperazinyl]carbonyl]-3-(4-morpholinyl)-3-oxopropyl]-, [S-(R\*,R\*)]- (9CI)  
 (CA INDEX NAME)

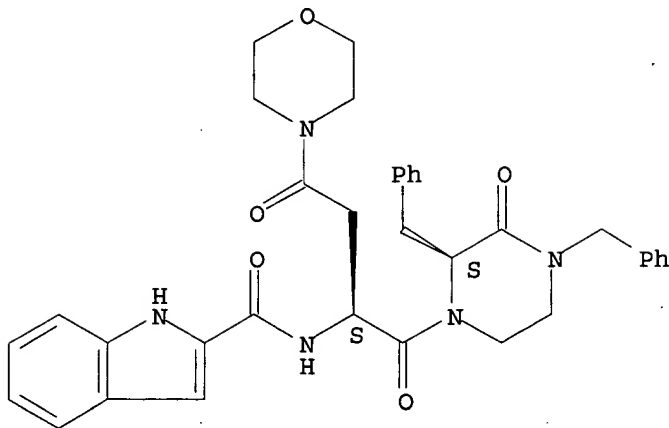
Absolute stereochemistry.



RN 204328-07-4 HCAPLUS

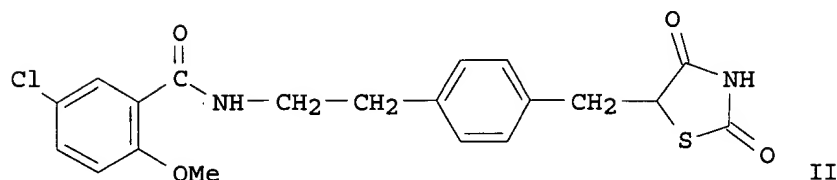
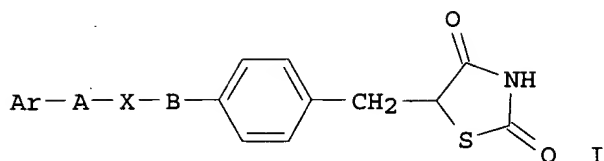
CN 1H-Indole-2-carboxamide, N-[3-(4-morpholinyl)-3-oxo-1-[[3-oxo-2,4-bis(phenylmethyl)-1-piperazinyl]carbonyl]propyl]-, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:275069 HCAPLUS  
 DOCUMENT NUMBER: 125:10799  
 TITLE: Thiazolidinedione compounds useful for treating  
 conditions of insulin-resistance and/or non  
 insulin-dependent **diabetes**  
 INVENTOR(S): Regnier, Gilbert; Charton, Yves; Duhault, Jacques;  
 Espinal, Joseph  
 PATENT ASSIGNEE(S): ADIR et Compagnie, Fr.  
 SOURCE: U.S., 6 pp., Cont.-in-part of U.S. Ser. No. 133,898,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5506245	A	19960409	US 1995-374970	19950119
FR 2696743	A1	19940415	FR 1992-12123	19921012
FR 2696743	B1	19941223		
PRIORITY APPLN. INFO.:			FR 1992-12123	19921012
			US 1993-133898	19931012
OTHER SOURCE(S):			MARPAT 125:10799	
GI				



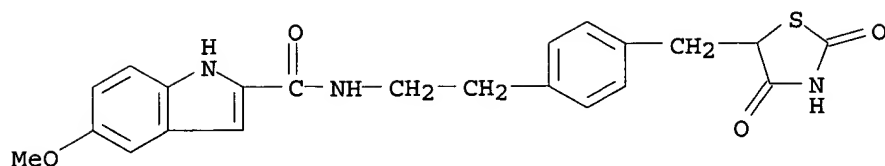
AB Thiazolidinedione compds. I useful for treating conditions of insulin-resistance and/or non insulin-dependent **diabetes** are provided, wherein: Ar represents a polymethylene ring, a mono-, bi- or tricyclic hydrocarbon radical, or a mono-, bi- or tri-cyclic heterocyclic radical contg. 1 or 2 hereto atoms selected from nitrogen, oxygen and sulfur atoms; A represents, e.g., a single bond, a hydrocarbon chain having 2 or 3 carbon atoms and including a double bond, or a chain of the formula  $(CH_2)_m$ ,  $O(CH_2)_m$  or  $S(CH_2)_m$  wherein: m is an integer from 1 to 3; X represents an oxygen atom, CONR or SO<sub>2</sub>NR wherein R represents a hydrogen atom or a straight-chain or branched alkyl radical having from 1 to 5 carbon atoms and optionally including a double bond, or, when A represents a single bond and Ar represents a Ph radical, R may also represent a carbonyl radical bonded to Ar by its free bond such that Ar-A-X together form a phthalimido radical; B represents a satd. hydrocarbon chain having from 1 to 6 carbon atoms which is optionally branched and/or substituted by a hydroxy radical or an oxo radical. Thus, e.g., cyclization of Me 3-{4-[2-(2-methoxy-5-chlorobenzamido)ethyl]phenyl}-2-chloropropionate with thiourea afforded 5-{4-[2-(2-methoxy-5-chlorobenzamido)ethyl]benzyl}thiazolidine-2,4-dione II which exhibited the same hypoglycemic effect at .ltoreq.10 mg/kg/day for 4 days as Ciglitazone at 50-100 mg/kg/day for 4 days. The compds. of the invention do not have any influence on the level of circulating glucose but decrease the level of triglycerides and free fatty acids in the plasma and also the level of immuno-reactive insulin.

IT 174772-17-9P 174772-25-9P

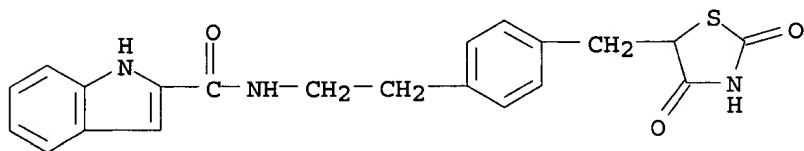
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(thiazolidinedione compds. useful for treating conditions of insulin-resistance and/or non insulin-dependent diabetes)

RN 174772-17-9 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]-5-methoxy- (9CI) (CA INDEX NAME)

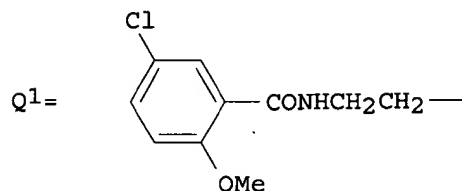
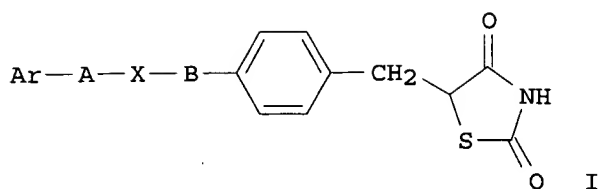


RN 174772-25-9 HCAPLUS  
 CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]- (9CI) (CA INDEX NAME)



L31 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2002 ACS  
 ACCESSION NUMBER: 1996:58393 HCAPLUS  
 DOCUMENT NUMBER: 124:232440  
 TITLE: Thazolidinedione compounds useful as antidiabetics  
 INVENTOR(S): Regnier, Gilbert; Charton, Yves; Duhault, Jacques; Espinal, Joseph  
 PATENT ASSIGNEE(S): Adir et Compagnie, Fr.  
 SOURCE: U.S., 7 pp. Cont.-in-part of U.S. Ser. No. 133,898, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5478853	A	19951226	US 1995-376052	19950120
FR 2696743	A1	19940415	FR 1992-12123	19921012
FR 2696743	B1	19941223		
PRIORITY APPLN. INFO.:			FR 1992-12123	19921012
			US 1993-133898	19931012
OTHER SOURCE(S):			MARPAT 124:232440	
GI				



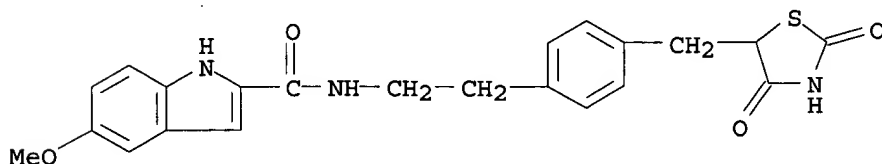
AB The title compds. are 5-(4-substituted benzyl)thiazolidine-2,4-diones I [Ar = polymethylene ring with optional alkyl substituent(s), (un)substituted aryl or heterocyclyl; A = bond, hydrocarbondiyl with double bond, (CH<sub>2</sub>)<sub>1-3</sub>, CMe<sub>2</sub>(CH<sub>2</sub>)<sub>0-2</sub>, (un)substituted CHPh(CH<sub>2</sub>)<sub>0-2</sub>, O(CH<sub>2</sub>)<sub>1-3</sub>, S(CH<sub>2</sub>)<sub>1-3</sub>; X = O, CONR, SO<sub>2</sub>NR; R = H, alkyl, alkenyl; or ArAX = phthalimido; B = satd. hydrocarbondiyl with optional OH or oxo substituent] and their enantiomers, diastereoisomers, and pharmaceutically tolerable salts. The compds. are useful for treating insulin resistance and/or non-insulin-dependent diabetes, possibly assocd. with hypertension. An exemplary compd. compd. is 5-[4-[2-(2-methoxy-5-chlorobenzamido)ethyl]benzyl]thiazolidine-2,4-dione, i.e., I [Ar-A-X-B- = Q1] (II), which was prepd. by cyclization of the corresponding 3-phenyl-2-chloropropionic acid deriv. with thiourea in sulfolane at 120.degree., followed by hydrolysis with aq. HCl at 100.degree.. II, at .ltoreq. 10 mg/kg/day orally in mice, had the same hypoglycemic effect as ciglitazone at 50-100 mg/kg/day. II also had little or no hematol. effect at 250 mg/kg/day in rats, whereas pioglitazone had strong adverse effects at 100 mg/kg/day.

IT 174772-17-9P 174772-25-9P

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of thiazolidinediones as antidiabetics)

RN 174772-17-9 HCAPLUS

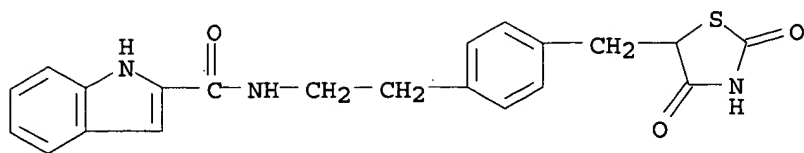
CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]-5-methoxy- (9CI) (CA INDEX NAME)



RN 174772-25-9 HCAPLUS

CN 1H-Indole-2-carboxamide, N-[2-[4-[(2,4-dioxo-5-thiazolidinyl)methyl]phenyl]ethyl]- (9CI) (CA INDEX NAME)





L31 ANSWER 28 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1994:410003 HCAPLUS

DOCUMENT NUMBER: 121:10003

TITLE: Preparation of peptides by reaction of olefinic alcohol and enol ether for treatment of tachypnea and myocardial reperfusion injury.

INVENTOR(S): Itsumi, Keiji; Kei, Seihaku; Fukami, Jikiki; Hashihon, Sanashi

PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 131 pp.

CODEN: JKXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

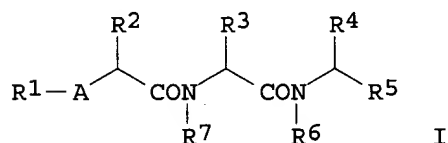
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 05208914	A2	19930820	JP 1992-233604	19920901
US 5430022	A	19950704	US 1993-86094	19930706
US 5656604	A	19970812	US 1995-422944	19950417
PRIORITY APPLN. INFO.:			US 1991-753997	19910903
			GB 1990-10740	19900514
			GB 1990-26254	19901203
			GB 1991-4064	19910227
			US 1991-696701	19910507
			US 1992-845056	19920303
			US 1993-86094	19930706

OTHER SOURCE(S): MARPAT 121:10003

GI



AB Title compds. I [R1 = H, acyl; R2 = alkyl, (un)substituted aralkyl, cycloalkylalkyl, (un)substituted heterocyclalkyl; R3 = (un)substituted heterocyclalkyl, (un)substituted aralkyl; R4 = H, (un)substituted alkyl; R5 = carboxy, (un)protected carboxy, (un)protected carboxyalkyl; R6 = H, (un)substituted alkyl; R7 = H, alkyl; A = O, NH, alkylimino, alkylene; with provisos], useful for the treatment of many cardiovascular injury, e.g., hypertension, are prepd. Thus, a mixt. of N-phenylacetyl-Leu-OH and H-D-Trp(Me)-D-Phe-OMe.HCl in DMF was stirred with ice cooling for 4.5 h to give PhCH2CO-Leu-D-Trp(Me)-D-Phe-OMe. In an in vitro study, Q-Leu-D-Trp(Me)-D-Pya-OH.HCl [Q = cyclohexylcarbamoyl, Pya = 2-pyridylalanine] (also prepd.) had an IC50 of 2.3.times.10<sup>-9</sup> M against

the binding of 125-I-endothelin-1 with pig aorta receptors.

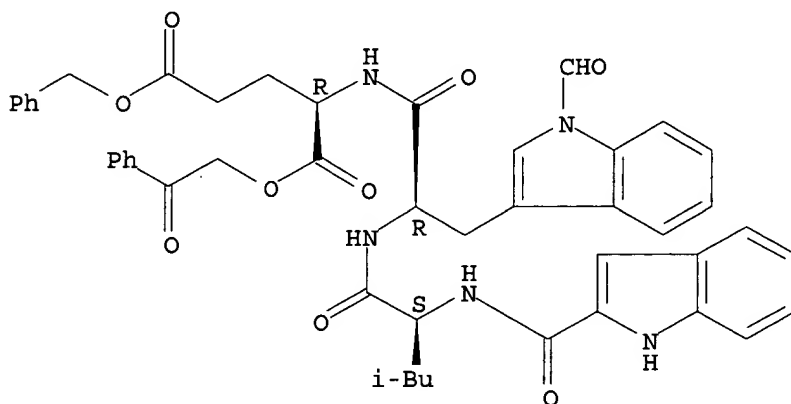
IT 142377-52-4P 142378-01-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of, for treatment of tachypnea and myocardial reperfusion injury)

RN 142377-52-4 HCAPLUS

CN D-Glutamic acid, N-[1-formyl-N-[N-(1H-indol-2-ylcarbonyl)-L-leucyl]-D-tryptophyl]-, 1-(2-oxo-2-phenylethyl) 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

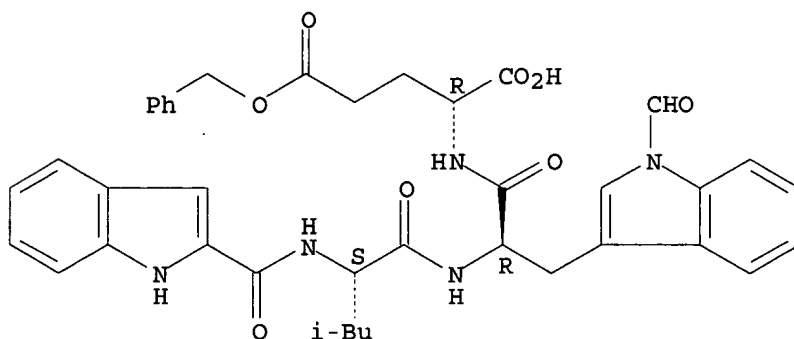
Absolute stereochemistry.



RN 142378-01-6 HCAPLUS

CN D-Glutamic acid, N-[1-formyl-N-[N-(1H-indol-2-ylcarbonyl)-L-leucyl]-D-tryptophyl]-, 5-(phenylmethyl) ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L31 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1993:409168 HCAPLUS

DOCUMENT NUMBER: 119:9168

TITLE: Preparation of oxiranyl and oxetanyl renin inhibiting compounds

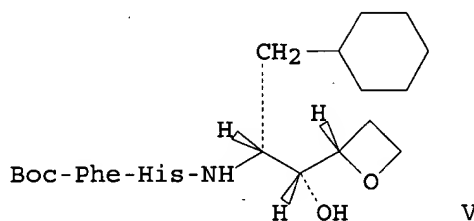
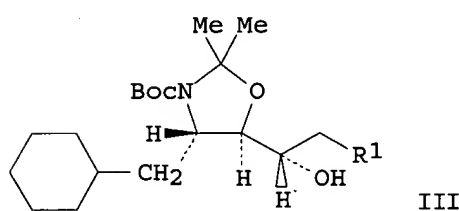
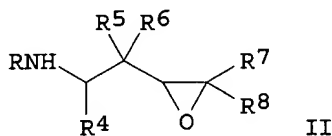
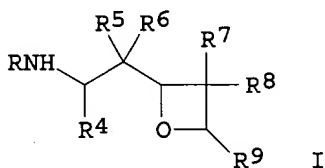
INVENTOR(S): Rosenberg, Saul H.

PATENT ASSIGNEE(S): Abbott Laboratories, USA

SOURCE: PCT Int. Appl., 168 pp.

DOCUMENT TYPE: CODEN: PIXXD2  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: 1 English  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9222313	A1	19921223	WO 1992-US4423	19920526
W: AU, CA, JP, KR				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
US 5258362	A	19931102	US 1992-880250	19920513
AU 9221593	A1	19930112	AU 1992-21593	19920526
PRIORITY APPLN. INFO.:			US 1991-713475	19910611
			US 1992-880250	19920513
			WO 1992-US4423	19920526
OTHER SOURCE(S):		MARPAT 119:9168		
GI				



AB The title compds. I and II [R = mimic of Phe-His dipeptide; R4 = lower alkyl, cycloalkyl, arylalkyl; R5 = H, lower alkyl, hydroxyalkyl, lower alkenyl, CHO; R6 = OH, NH2; R7 = H, lower alkyl; R8 = H, lower alkyl, hydroxyalkyl, alkoxyalkyl, thioalkoxyalkyl, haloalkyl, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, cycloalkyl, cycloalkylalkyl, lower alkenyl, alkynyl, aryl, arylalkyl, heterocyclic, heterocycloalkyl; R7R8 = (CH2)<sub>n</sub>, n = 3-6; R9 = lower alkyl] or a pharmaceutically acceptable salt, ester, or prodrug of, were prepd. as renin inhibitors. Thus, Reformatskii reaction of (4S,5R)-3-tert-butoxycarbonyl-4-cyclohexylmethyl-2,2-dimethyloxazolidine-5-carboxaldehyde with benzyl bromoacetate gave hydroxy ester III (Boc = Me<sub>3</sub>CO<sub>2</sub>C; R1 = CO<sub>2</sub>CH<sub>2</sub>Ph), which was reduced with NaBH<sub>4</sub>-CaCl<sub>2</sub> to diol III (R1 = CH<sub>2</sub>OH) and selectively tosylated to tosylate III (R1 = CH<sub>2</sub>OSOC<sub>6</sub>H<sub>4</sub>Me-4) (IV). Cyclization of tosylate IV to the corresponding oxetane, followed by acidic deprotection, coupling with Boc-Phe-His(Boc)-OH, and selective deblocking gave oxetanyl peptide V. Compds. I and II are useful in treating hypertension, congestive heart failure, glaucoma, and inhibiting HIV-1 and HIV-2 proteases.

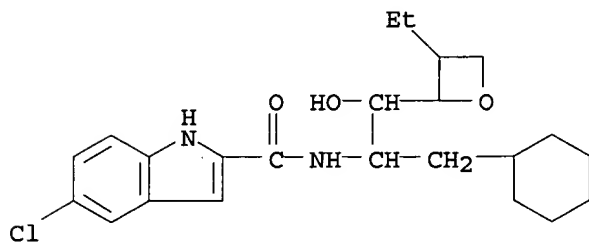
IT 147896-46-6P

RL: BAC (Biological activity or effector, except adverse); SPN

(Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(prepn. of, as renin inhibitor)

RN 147896-46-6 HCAPLUS

CN L-Altritol, 4,6-anhydro-2-[[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-1-cyclohexyl-1,2,5-trideoxy-5-ethyl- (9CI) (CA INDEX NAME)



L31 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1988:493611 HCAPLUS

DOCUMENT NUMBER: 109:93611

TITLE: Preparation and testing of  
(aminopropoxy)naphthylcarboxamidopentylalanylprolines  
and indole analogs as **cardiovascular** agents

INVENTOR(S): Allan, Geoffrey; Hardy, George William; Bull, Donald;  
Mills, Gail; Lee, Grahame Roy

PATENT ASSIGNEE(S): Wellcome Foundation Ltd., UK

SOURCE: Eur. Pat. Appl., 43 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 234946	A2	19870902	EP 1987-301740	19870227
EP 234946	A3	19880817		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8700872	A	19870829	FI 1987-872	19870227
DK 8701033	A	19870829	DK 1987-1033	19870227
AU 8769536	A1	19870903	AU 1987-69536	19870227
JP 62252799	A2	19871104	JP 1987-45119	19870227
HU 46045	A2	19880928	HU 1987-816	19870227
ZA 8701454	A	19881026	ZA 1987-1454	19870227
DD 263052	A5	19881221	DD 1987-300269	19870227

PRIORITY APPLN. INFO.:

GB 1986-5049 19860228

GB 1986-20767 19860828

AB Me<sub>2</sub>CHNHCH<sub>2</sub>CH(OH)CH<sub>2</sub>OXCONH(CH<sub>2</sub>)<sub>4</sub>CHZNHCHMeCOY (I; X = naphthyl, indolyl ring system; Y = CO<sub>2</sub>H, C<sub>2</sub>-5 alkoxy carbonyl; Z = carboxypyrrolidinyl) were prepd. as antihypertensives. Me 4-hydroxyindole-2-carboxylate (prepn. given) was treated with NaH in DMF and 2S-glycidyl tosylate was added at 0.degree.. The mixt. was stirred 3 h at 50.degree. to give the 4-oxiranylmethoxy compd., which was heated with Me<sub>2</sub>CHNH<sub>2</sub> in DMF/H<sub>2</sub>O to give Me 4-[2(S)-hydroxy-3-isopropylamino]-1H-indole-2-carboxylate. The latter was N-protected, sapond., coupled with tert-Bu N-[1(S)-tert-butoxycarbonyl-5-aminopentyl]-(S)alanyl-(S)-proline (prepn. given) to give N-1S-carboxy-5-[4-(2S-hydroxy-3-isopropylaminopropoxy)-1H-indol-2-ylcarboxamido]pentyl-S-alanyl-S-proline. The latter inhibited ACE in a

test of angiotensin-I-induced pig ileum contractility with an EC50 of 1.4 nM.

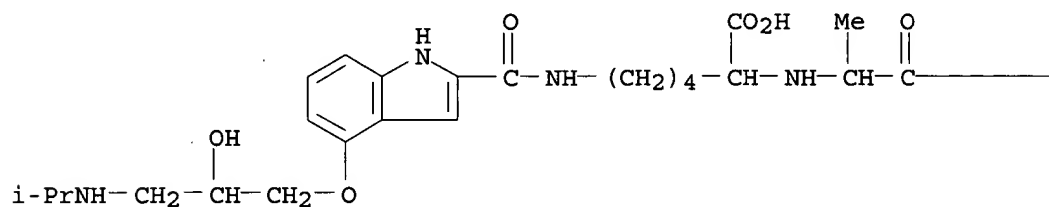
IT 115794-86-0P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of, as cardiovascular agent)

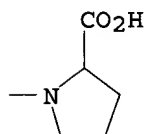
RN 115794-86-0 HCAPLUS

CN L-Proline, N-[(1S)-1-carboxy-5-[[[4-[(2S)-2-hydroxy-3-[(1-methylethyl)amino]propoxy]-1H-indol-2-yl]carbonyl]amino]pentyl]-L-alanyl-(9CI) (CA INDEX NAME)

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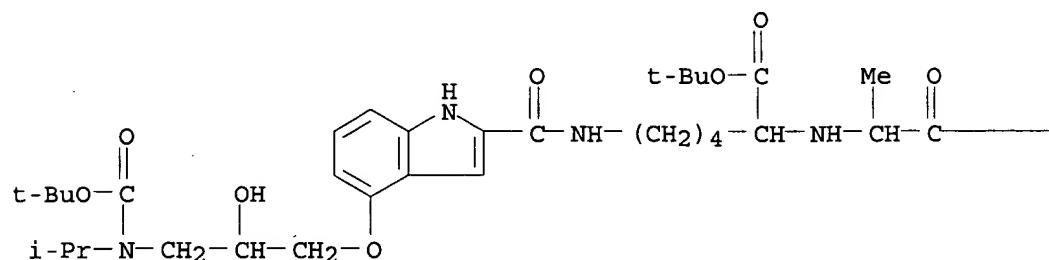
IT 115794-89-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as intermediate for cardiovascular agent)

RN 115794-89-3 HCAPLUS

CN L-Proline, 1-[N-[1-[(1,1-dimethylethoxy)carbonyl]-5-[[[4-[3-[(1,1-dimethylethoxy)carbonyl](1-methylethyl)amino]-2-hydroxypropoxy]-1H-indol-2-yl]carbonyl]amino]pentyl]-L-alanyl]-, 1,1-dimethylethyl ester, [S-(R\*,R\*)]- (9CI) (CA INDEX NAME)

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